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NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
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NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	JAN 11	CA/CAPLUS - Expanded patent coverage to include Russia (Federal Institute of Industrial Property)

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=> file caplus hcalplu
'HCALPLU' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):caplus hcaplus
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.21       0.21

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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=> s jnk (w) inhbit?
L1            0 JNK (W) INHBIT?

=> s jnk (p) inhbit?
L2            0 JNK (P) INHBIT?

=> JNK
JNK IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> S JNK
L3        12276 JNK

=> S L3 AND (atherosclerosis or restenosis or angioplasty or hypertrophy or
diabetes or esteoporosis or electile or cachexia or infarction or ischem? or
transplant or endotoxin)
L4         1278 L3 AND (ATHEROSCLEROSIS OR RESTENOSIS OR ANGIOPLASTY OR HYPERTRO
                PHY OR DIABETES OR ESTEOPOROSIS OR ELECTILE OR CACHEXIA OR INFAR
                CTION OR ISCHEM? OR TRANSPLANT OR ENDOTOXIN)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           639 DUP REM L4 (639 DUPLICATES REMOVED)

=> s l5 and pd<2000
L6           102 L5 AND PD<2000

=> d l6 1-102 bib,kwic

L6   ANSWER 1 OF 102  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2000:125483  CAPLUS
DN   132:263742
TI   Complement activation and atherosclerosis
AU   Niculescu, Florin; Rus, Horea
CS   Department of Pathology, School of Medicine, University of Maryland,
     Baltimore, MD, 21201, USA
SO   Molecular Immunology (1999), 36(13-14), 949-955
```

CODEN: MOIMD5; ISSN: 0161-5890
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Complement activation and **atherosclerosis**
SO Molecular Immunology (**1999**), 36(13-14), 949-955
CODEN: MOIMD5; ISSN: 0161-5890
AB A review with 59 refs. **Atherosclerosis** is an inflammatory disease mediated via the action of monocyte/macrophages, complement, and T-cells. C5a and monocyte chemotactic factor released during complement activation in the arterial wall may participate in the initial monocyte recruitment. Assembly of C5b-9 on cells of the arterial wall may also induce cell lysis. Sublytic assembly of C5b-9 on smooth muscle cells (SMC) and endothelial cells (EC) induces cell activation and proliferation. Anal. of mitogen activated protein kinases (MAPK) pathways induced by C5b-9 in aortic SMC revealed that extracellular signal regulated kinase (ERK) 1, c-jun NH2-terminal kinase (**JNK**) 1, and p38 MAPK are all activated by C5b-9. ERK1 activity was inhibited by wortmannin suggesting that ERK1 pathway is activated through phosphatidylinositol-3 kinase. Sublytic C5b-9 assembly on the plasma membrane was also able to activate Janus kinase (JAK) 1, signal transducer and activator (STAT) 3, and STAT4 in EC. JAK1 but not STAT3 activation induced by C5b-9 is dependent on Gi protein activation. New evidence accumulated during the last decade supports the role of complement activation in both initiation and progression of the atherosclerotic lesions. Complement system activation is a major component of the chronic inflammatory process associated with **atherosclerosis**.
ST complement activation **atherosclerosis** review
IT Complement
(activation; complement activation and **atherosclerosis**)
IT **Atherosclerosis**
(complement activation and **atherosclerosis**)
IT Signal transduction, biological
(pathways; complement activation and **atherosclerosis**)

L6 ANSWER 2 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:65157 CAPLUS
DN 132:342575
TI The activation of the **JNK**/c-Jun axis and expression of the Fas-Ligand following focal **ischemia** are prevented by the immunosuppressant FK506
AU Brecht, S.; Mielke, K.; Yu, M. H.; Herdegen, T.
CS Germany
SO Pharmacology of Cerebral Ischemia 1998, [International Symposium on Pharmacology of Cerebral Ischemia], 7th, Marburg, July 27-29, 1998 (**1999**), Meeting Date 1998, 151-159. Editor(s): Krieglstein, Josef. Publisher: Medpharm Scientific Publishers, Stuttgart, Germany.
CODEN: 68OZA5
DT Conference; General Review
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI The activation of the **JNK**/c-Jun axis and expression of the Fas-Ligand following focal **ischemia** are prevented by the immunosuppressant FK506
SO Pharmacology of Cerebral Ischemia 1998, [International Symposium on Pharmacology of Cerebral Ischemia], 7th, Marburg, July 27-29, 1998 (**1999**), Meeting Date 1998, 151-159. Editor(s): Krieglstein, Josef. Publisher: Medpharm Scientific Publishers, Stuttgart, Germany.
CODEN: 68OZA5

AB A review with 26 refs. of the authors work analyzing the following questions: (1) Does **ischemic** injury result in N-terminal phosphorylation of c-Jun and activation of **JNK** (2) Is the N-terminal phosphorylation of c-Jun linked with the appearance of TUNEL, a marker for apoptotic death, and (3) with the expression of Fas-Ligand and (4) To which extent does FK506 interfere with these alterations. Following 90 min occlusion of the MCA in the adult rat: (i) the transcription factor c-Jun is N-terminally phosphorylated in the areas adjacent to the **ischemic** core, and phosphorylation of c-Jun is closely linked to the presence of TUNEL labeling, (ii) the constitutive transcription factor ATF-2 is downregulated in the infarcted hemisphere, (iii) **JNK** activity and expression are transiently increased and (iv) Fas-Ligand is expressed in neurons around the **ischemic** core. (v) Finally, FK506 significantly reduces the infarct area and prevents both, the phosphorylation of c-Jun, the expression of Fas-Ligand and the occurrence of TUNEL.

ST review **JNK** cJun Fas Ligand focal **ischemia** immunosuppressant FK506

IT Anti-**ischemic** agents
Immunosuppressants
(activation of **JNK**/c-Jun axis and expression of Fas-Ligand following focal **ischemia** are prevented by immunosuppressant FK506)

IT Fas ligand
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of **JNK**/c-Jun axis and expression of Fas-Ligand following focal **ischemia** are prevented by immunosuppressant FK506)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-jun; activation of **JNK**/c-Jun axis and expression of Fas-Ligand following focal **ischemia** are prevented by immunosuppressant FK506)

IT Brain, disease
(**ischemia**, focal; activation of **JNK**/c-Jun axis and expression of Fas-Ligand following focal **ischemia** are prevented by immunosuppressant FK506)

IT 104987-11-3, FK506
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activation of **JNK**/c-Jun axis and expression of Fas-Ligand following focal **ischemia** are prevented by immunosuppressant FK506)

IT 155215-87-5, c-Jun amino-terminal kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of **JNK**/c-Jun axis and expression of Fas-Ligand following focal **ischemia** are prevented by immunosuppressant FK506)

L6 ANSWER 3 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:11289 CAPLUS
DN 132:150083
TI MEKK1 suppresses oxidative stress-induced apoptosis of embryonic stem cell-derived cardiac myocytes
AU Minamino, Tetsuo; Yujiri, Toshiaki; Papst, Philip J.; Chan, Edward D.; Johnson, Gary L.; Terada, Naohiro
CS Program in Molecular Signal Transduction, Division of Basic Sciences, Department of Pediatrics, National Jewish Medical and Research Center,

Denver, CO, 80206, USA
SO Proceedings of the National Academy of Sciences of the United States of America (**1999**), 96(26), 15127-15132
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Proceedings of the National Academy of Sciences of the United States of America (**1999**), 96(26), 15127-15132
CODEN: PNASA6; ISSN: 0027-8424
AB A combination of in vitro embryonic stem (ES) cell differentiation and targeted gene disruption has defined complex regulatory events underlying oxidative stress-induced cardiac apoptosis, a model of postischemic reperfusion injury of myocardium. ES cell-derived cardiac myocytes (ESCM) having targeted disruption of the MEKK1 gene were extremely sensitive, relative to wild-type ESCM, to hydrogen peroxide-induced apoptosis. In response to oxidative stress, MEKK1-/- ESCM failed to activate c-Jun kinase (**JNK**) but did activate p38 kinase similar to that observed in wild-type ESCM. The increased apoptosis was mediated through enhanced tumor necrosis factor α production, a response that was pos. and neg. regulated by p38 and the MEKK1-**JNK** pathway, resp. Thus, MEKK1 functions in the survival of cardiac myocytes by inhibiting the production of a proapoptotic cytokine. MEKK1 regulation of the **JNK** pathway is a critical response for the protection against oxidative stress-induced apoptosis in cardiac myocytes.
IT Apoptosis
Oxidative stress, biological
(MEKK1 suppresses oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)
IT Reactive oxygen species
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(MEKK1 suppresses oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)
IT Signal transduction, biological
(for MEKK1 suppression of oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)
IT Reperfusion
(injury; MEKK1 suppresses oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)
IT Heart, disease
(**ischemia**; MEKK1 suppresses oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)
IT Heart
(myocyte; MEKK1 suppresses oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)
IT 146702-84-3, MEK kinase 1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MEKK1 suppresses oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)
IT 155215-87-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in signal transduction pathway for MEKK1 suppression of oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)
IT 165245-96-5, p38 MAP kinase
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(in signal transduction pathway for tumor necrosis factor-mediated

oxidative stress-induced apoptosis of cardiac myocytes in **ischemia**-reperfusion injury model)

L6 ANSWER 4 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:805141 CAPLUS
DN 132:91836
TI Increased **JNK**, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling
AU Takemoto, Yasuhiko; Yoshiyama, Minoru; Takeuchi, Kazuhide; Omura, Takashi; Komatsu, Ryuji; Izumi, Yasukatsu; Kim, Shokei; Yoshikawa, Junichi
CS First Department of Internal Medicine, Osaka City University Medical School, Osaka, 545-8585, Japan
SO Journal of Molecular and Cellular Cardiology (**1999**), 31(11), 2017-2030
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic Press
DT Journal
LA English
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Increased **JNK**, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling
SO Journal of Molecular and Cellular Cardiology (**1999**), 31(11), 2017-2030
CODEN: JMCDAY; ISSN: 0022-2828
AB The in vivo signal transduction pathway, responsible for isoproterenol-induced cardiac **hypertrophy** or remodeling, remains to be clarified. The purpose of this study was to examine c-Jun NH2-terminal kinase (**JNK**) and extracellular signal-regulated kinase (ERK), activator protein-1 (AP-1) and nuclear factor-κB (NK-κB) DNA binding activity, which seem to be important in a signal transduction cascade upstream of the increased level of mRNA expression observed in isoproterenol-induced cardiac remodeling. Rats were continuously infused with saline and isoproterenol by i.v. injection (a short period: 0.5 μg/kg/min) and an osmotic minipump (a long period: 0.5 or 3 mg/kg/day). Cardiac morphol. was measured by echocardiog. **JNK** and ERK were measured by in gel kinase assay. AP-1 and NF-κB DNA binding activity was determined using an electrophoretic mobility shift assay. Echocardiogram showed that the thickness of the left ventricular anterior wall (AW) and left ventricular posterior wall (PW) increased at day 1 in low doses, and at day 1 in high doses. Isoproterenol significantly increased ERK and **JNK** activity at 15 min after i.v. infusion of 0.5 μg/kg/min isoproterenol. At late phase about **JNK** and ERK activity, only a high dose of isoproterenol increased **JNK**. AP-1 DNA binding activities spurred by low or high doses of isoproterenol administration increased at 12 h. reached their peak of 24.1- and 37.1-fold ($P<0.01$), resp., at 24 h, and thereafter decreased. Although low doses of isoproterenol did not change the level of NF-κB DNA binding activities, high doses increased it to 10.9-fold ($P<0.01$) at day 2. This study showed increased **JNK**, ERK, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling. AP-1 may contribute to the isoproterenol-induced cardiac remodeling, and **JNK** or NF-κB may also play some roles in it. (c) 1999 Academic Press.
ST isoproterenol heart **hypertrophy** transcription factor NFKB; cardiac remodeling isoproterenol **JNK** AP1
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1); increased **JNK**, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-κB (nuclear factor κB); increased **JNK**, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling)
IT Heart, disease
(**hypertrophy**; increased **JNK**, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling)
IT Signal transduction, biological
(increased **JNK**, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling)
IT 7683-59-2, Isoproterenol
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(increased **JNK**, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling)
IT 137632-07-6 137632-08-7 155215-87-5, c-Jun amino-terminal kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(increased **JNK**, AP-1 and NF-κB DNA binding activities in isoproterenol-induced cardiac remodeling)

L6 ANSWER 5 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:790069 CAPLUS
DN 132:235257
TI Activation of the **JNK** pathway is important for cardiomyocyte death in response to simulated **ischemia**
AU He, Huaping; Li, Hai-Ling; Lin, Anning; Gottlieb, Roberta A.
CS Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Cell Death and Differentiation (**1999**), 6(10), 987-991
CODEN: CDDIEK; ISSN: 1350-9047
PB Stockton Press
DT Journal
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Activation of the **JNK** pathway is important for cardiomyocyte death in response to simulated **ischemia**
SO Cell Death and Differentiation (**1999**), 6(10), 987-991
CODEN: CDDIEK; ISSN: 1350-9047
AB Multiple signaling pathways, including the c-Jun N-terminal kinase (**JNK**) pathway, are activated in myocardial **ischemia** and reperfusion (MI/R) and correlate with cell death. However, the role of the **JNK** pathway in MI/R-induced cell death is poorly understood. In a rabbit model, we found that **ischemia** followed by reperfusion resulted in **JNK** activation which could be detected in cytosol as well as in mitochondria. To address the functional role of the **JNK** activation, we examined the consequences of blockade of **JNK** activation in isolated cardiomyocytes under conditions of simulated **ischemia**. The **JNK** activity was stimulated .apprx. sixfold by simulated **ischemia** and reperfusion (simulated MI). When a dominant neg. mutant of **JNK** kinase-2 (dnJNKK2), an upstream regulator of **JNK**, and **JNK**-interacting protein-1 (JIP-1) were expressed in myocytes by recombinant adenovirus, the activation of **JNK** by simulated MI was reduced 53%. Furthermore, the TNFα-activated **JNK** activity in H9c2 cells was completely abolished by dnJNKK2 and JIP-1. In correlation, when dnJNKK2 and JIP-1 were expressed in cardiomyocytes, both constructs significantly reduced cell death after simulated MI compared to vector

controls. Apparently, activation of the **JNK** cascade is important for cardiomyocyte death in response to simulated **ischemia**.

ST cardiomyocyte death **ischemia** Jun kinase

IT Cell death
Ischemia
(activation of the **JNK** pathway is important for cardiomyocyte death in response to simulated **ischemia**)

IT Heart
(myocyte; activation of the **JNK** pathway is important for cardiomyocyte death in response to simulated **ischemia**)

IT 155215-87-5, c-Jun N-terminal kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of the **JNK** pathway is important for cardiomyocyte death in response to simulated **ischemia**)

L6 ANSWER 6 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:771994 CAPLUS
DN 132:220652
TI Mesangial cell signaling cascades in response to mechanical strain and glucose
AU Ingram, Alistair John; Ly, Hao; Thai, Kerri; Kang, Myung-Jae; Scholey, James W.
CS Department of Medicine, McMaster University, Hamilton, ON, Can.
SO Kidney International (**1999**), 56(5), 1721-1728
CODEN: KDYIA5; ISSN: 0085-2538
PB Blackwell Science, Inc.
DT Journal
LA English
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Kidney International (**1999**), 56(5), 1721-1728
CODEN: KDYIA5; ISSN: 0085-2538
AB Elevated glucose levels and glomerular hypertension (Pgc) are considered to contribute to the elaboration of matrix protein by mesangial cells (MCs) in diabetic glomeruli. MCs grown in 30 mM of glucose produce excessive matrix protein, as do MCs exposed to cyclic strain, and the combination of the 2 exacerbates this. Tight glucose control or reduction in Pgc clin. delays progression of diabetic nephropathy. MC c-fos is induced in response to either application of strain or high ambient glucose, inducing increases in activated protein-1 transactivational activity and extracellular matrix production Stimuli that lead to c-fos induction pass through the 3 mitogen-activated protein (MAP) kinase pathways: p44/42, SAPK/**JNK**, and p38/HOG. The authors studied MAP kinase activation in MCs exposed to mech. strain and a high glucose. MCs (passage 5 through 10) cultured for 96 h on type 1 collagen-coated flexible-bottom plates in either 5.6 or 30 mM glucose were exposed to 5, 10, or 30 min of cyclic strain (60 cycles per min) by computer-driven generation of vacuums of -14 kPa, inducing 20% elongation in the diameter of the surface. Control MCs were grown on both coated rigid and flexible-bottom plates. Protein levels (by Western blot) and activity assays for all 3 kinase cascades were performed at baseline and after 5, 10, and 30 min. All expts. were performed in triplicate. MAP kinase signaling was seen in response to stretch, and high ambient glucose affected the pattern of activation. Both p44/42 and p38HOG kinase activities showed small increases to a maximum of 2.5- to 3.5-fold greater than static MCs at 10 min. Activity in both kinase cascades was slightly suppressed by 30 mM glucose. In contrast, SAPK/**JNK** activity was present at a very low level in static MCs and increased markedly by 10 min of stretch. 30 Micromolars of glucose augmented this effect by a factor of 6 over MCs cultured in 5.6 mM glucose after 10 min of stretch. Neither

glucose concentration nor mech. strain had any effect on the protein expression of any of the kinases by Western blot. Thus, MAP kinase cascade signaling is seen when phys. force is applied to MCs, and glucose affects the pattern of activity. 30 Micromolars of glucose markedly increase the level of SAPK/**JNK** activation. This may have implications in diabetic signal transduction and matrix protein production

ST **diabetes** nephropathy mesangium glucose kinase signaling; MAP kinase signaling **diabetes** nephropathy mesangium glucose

IT 155215-87-5, **JNK** kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**JNK** and SAP kinase activity and expression in mesangial cell in response to mech. strain and glucose in diabetic nephropathy)

L6 ANSWER 7 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:768819 CAPLUS
DN 132:76954
TI PKC-dependent activation of p46/p54 JNKs during **ischemic** preconditioning in conscious rabbits
AU Ping, Peipei; Zhang, Jun; Huang, Shuang; Cao, Xinan; Tang, Xian-Liang; Li, Richard C. X.; Zheng, Yu-Ting; Qiu, Yumin; Clerk, Angela; Sugden, Peter; Han, Jiahuai; Bolli, Roberto
CS Experimental Research Laboratory, Division of Cardiology, University of Louisville, Louisville, KY, 40202, USA
SO American Journal of Physiology (**1999**), 277(5, Pt. 2), H1771-H1785
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI PKC-dependent activation of p46/p54 JNKs during **ischemic** preconditioning in conscious rabbits
SO American Journal of Physiology (**1999**), 277(5, Pt. 2), H1771-H1785
CODEN: AJPHAP; ISSN: 0002-9513
AB A conscious rabbit model was used to study the effect of **ischemic** preconditioning (PC) on stress-activated kinases [c-Jun NH2-terminal kinases (JNKs) and p38 mitogen-activated protein kinase (MAPK)] in an environment free of surgical trauma and attending external stress. **Ischemic** PC (6 cycles of 4-min **ischemia**/4-min reperfusion) induced significant activation of protein kinase C (PKC)-ε in the particulate fraction, which was associated with activation of p46 **JNK** in the nuclear fraction and p54 **JNK** in the cytosolic fraction; all of these changes were completely abolished by the PKC inhibitor chelerythrine. Selective enhancement of PKC-ε activity in adult rabbit cardiac myocytes resulted in enhanced activity of p46/p54 JNKs, providing direct in vitro evidence that PKC-ε is coupled to both kinases. Studies in rabbits showed that the activation of p46 **JNK** occurred during **ischemia**, whereas that of p54 **JNK** occurred after reperfusion. A single 4-min period of **ischemia** induced a robust activation of the p38 MAPK cascade, which, however, was attenuated after 5 min of reperfusion and disappeared after six cycles of 4-min **ischemia**/reperfusion. Overexpression of PKC-ε in cardiac myocytes failed to increase the p38 MAPK activity. These results demonstrate that **ischemic** PC activates p46 and p54 JNKs via a PKC-ε-dependent signaling pathway and that there are important differences between p46 and p54 JNKs with respect to the subcellular compartment (cytosolic vs. nuclear) and the mechanism (**ischemia**

vs. reperfusion) of their activation after **ischemic** PC.
ST protein kinase C **JNK** heart **ischemia** preconditioning
IT Signal transduction, biological
(PKC-dependent activation of p46/p54 JNKs during **ischemic** preconditioning in conscious rabbits)
IT Heart, disease
(**ischemia**; PKC-dependent activation of p46/p54 JNKs during **ischemic** preconditioning in conscious rabbits)
IT Phosphorylation, biological
(protein; PKC-dependent activation of p46/p54 JNKs during **ischemic** preconditioning in conscious rabbits)
IT 155215-87-5 165245-96-5, p38 Mitogen-activated protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PKC-dependent activation of p46/p54 JNKs during **ischemic** preconditioning in conscious rabbits)
IT 141436-78-4, Protein kinase C
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ε; PKC-dependent activation of p46/p54 JNKs during **ischemic** preconditioning in conscious rabbits)

L6 ANSWER 8 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:765968 CAPLUS
DN 132:73230
TI Inhibition of **endotoxin**-induced TNF-α production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones
AU Rawlins, Philip; Mander, Thomas; Sadeghi, Roya; Hill, Simon; Gammon, Guy; Foxwell, Brian; Wrigley, Stephen; Moore, Michael
CS Xenova Ltd, Slough, SL1 4EF, UK
SO International Journal of Immunopharmacology (**1999**), 21(12), 799-814
CODEN: IJIMDS; ISSN: 0192-0561
PB Elsevier Science Ltd.
DT Journal
LA English
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Inhibition of **endotoxin**-induced TNF-α production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones
SO International Journal of Immunopharmacology (**1999**), 21(12), 799-814
CODEN: IJIMDS; ISSN: 0192-0561
ST resorcylic lactone **endotoxin** inflammatory cytokine signaling; mitogen activated protein kinase resorcylic lactone
IT Lipopolysaccharides
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(bacterial; inhibition of **endotoxin**-induced inflammatory cytokine production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones)
IT Estrogen receptors
Glucocorticoid receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding to; inhibition of **endotoxin**-induced inflammatory cytokine production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones)
IT Macrophage
Monocyte
Signal transduction, biological
Structure-activity relationship

(inhibition of **endotoxin**-induced inflammatory cytokine production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones)

IT Interleukin 1β
Interleukin 6
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of **endotoxin**-induced inflammatory cytokine production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones)

IT Lactones
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(resorcylic acid; inhibition of **endotoxin**-induced inflammatory cytokine production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones)

IT 10497-39-9 12772-57-5, Monorden 17924-92-4, Zearalenone 66018-38-0 69427-14-1, Zeaenol 160191-26-4 253863-19-3 253863-20-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of **endotoxin**-induced inflammatory cytokine production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones)

IT 137632-07-6, P44 MAP kinase 137632-08-7, p42Map Kinase 141349-87-3, p55fyn Kinase 155215-87-5, **JNK** protein kinase 165245-96-5, p38 MAP kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of **endotoxin**-induced inflammatory cytokine production in macrophages by 5Z-7-oxo-zeaenol and other fungal resorcylic acid lactones)

L6 ANSWER 9 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:762268 CAPLUS
DN 132:106433
TI Expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**
AU Gillardon, F.; Spranger, M.; Tiesler, C.; Hossmann, K.-A.
CS Max-Planck-Institut fur Neurologische Forschung, Koln, Germany
SO Molecular Brain Research (**1999**), 73(1,2), 138-143
CODEN: MBREE4; ISSN: 0169-328X
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**
SO Molecular Brain Research (**1999**), 73(1,2), 138-143
CODEN: MBREE4; ISSN: 0169-328X
AB Persistent activation of c-Jun N-terminal kinases (JNKs) and phosphorylation of c-Jun has been shown in various cell death paradigms. Inhibition of the **JNK** signal transduction pathway prevented neuronal cell death both in vitro and in vivo. In the present study, nuclear phospho-c-Jun immunoreactivity became apparent selectively in vulnerable hippocampal CA1 neurons at 24 h after transient global cerebral **ischemia**. A high constitutive expression of phospho-JNK1 was detected by immunoblot anal. of hippocampal exts. Expression of **JNK** interacting protein-1 (JIP-1), which facilitates **JNK** signaling, remained unchanged in post-**ischemic** hippocampal neurons. By contrast, p53-activated gene 608 (PAG608), which promotes

cell death in vitro, was strongly induced in post-**ischemic** CA1 neurons. Our data suggest that transcription factors p53 and phospho-c-Jun may contribute to programmed CA1 cell death following **ischemia**.

ST brain **ischemia** hippocampus neuron Jun phosphorylation gene PAG608

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PAG608; expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

IT Nerve, disease
(death; expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

IT Signal transduction, biological
(expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

IT p53 (protein)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

IT Brain
(hippocampus, sector CA1; expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

IT Brain, disease
(**ischemia**; expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

IT Cell death
Cell death
(neuron; expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

IT Phosphorylation, biological
(protein, of **JNK** kinase; expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

IT 155215-87-5, c-Jun N-terminal kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(expression of cell death-associated phospho-c-Jun and p53-activated gene 608 in hippocampal CA1 neurons following global **ischemia**)

L6 ANSWER 10 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:690961 CAPLUS
DN 131:281581
TI Methods using a modulator of a MAPK/ERK, **JNK**, or p38 signal transduction pathway for treating and preventing insulin resistance and related disorders
IN Greenberg, Andrew S.
PA Trustees of Tufts College, USA
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9953927	A1	19991028	WO 1999-US8364	19990416 <--
	W: JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1071429	A1	20010131	EP 1999-917572	19990416
	EP 1071429	B1	20020130		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	AT 212552	E	20020215	AT 1999-917572	19990416
PRAI	US 1998-82152P	P	19980417		
	US 1998-82741P	P	19980423		
	WO 1999-US8364	W	19990416		

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Methods using a modulator of a MAPK/ERK, **JNK**, or p38 signal transduction pathway for treating and preventing insulin resistance and related disorders

PI WO 9953927 A1 **19991028**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9953927	A1	19991028	WO 1999-US8364	19990416 <--
	W: JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1071429	A1	20010131	EP 1999-917572	19990416
	EP 1071429	B1	20020130		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	AT 212552	E	20020215	AT 1999-917572	19990416

AB The invention provides methods, therapeutics, and kits for treating and preventing diseases or conditions associated with excessive lipolysis, in particular TNF-α induced lipolysis, and/or excessive free fatty acid levels. Exemplary conditions include insulin-resistance, **diabetes** (in particular, non-insulin-dependent **diabetes** mellitus), obesity, glucose intolerance, hyperinsulinemia, polycystic ovary syndrome, and coronary artery disease. In a preferred embodiment, the method includes administering to a subject in need a pharmaceutically effective amount of an inhibitor of the **JNK** signal transduction pathway and/or an inhibitor of the MAPK/ERK signal transduction pathway and/or a stimulator of the p38 signal transduction pathway.

ST signal transduction modulator TNF lipolysis disease; **JNK** pathway modulator TNF lipolysis disease; MAPK pathway modulator TNF lipolysis disease; ERK pathway modulator TNF lipolysis disease; p38 pathway modulator TNF lipolysis disease; insulin resistance treatment signal transduction modulator; **diabetes** obesity treatment signal transduction modulator; glucose intolerance treatment signal transduction modulator; hyperinsulinemia treatment signal transduction modulator; polycystic ovary syndrome treatment signal transduction modulator; coronary artery disease treatment signal transduction modulator

IT Mutation
(ERK1/2 or **JNK**; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ERK1/2 or **JNK**; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Adipose tissue
Antidiabetic agents

Drug screening
Signal transduction, biological
(MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Tumor necrosis factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Ribozymes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Fatty acids, biological studies
Interleukin 6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Obesity
(TNF-α level and; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Adipose tissue
(adipocyte; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Nucleic acids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense and triplex; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Gene
(expression; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Lipids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(lipolysis; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(perilipin A and B; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Phosphorylation, biological
(protein; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

IT Peroxisome proliferator-activated receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(γ; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced

lipolysis)
IT 152121-47-6, SB203580
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)
IT 54-21-7, Sodium salicylate 87893-55-8, 15-Deoxy-Δ12,14-PGJ2 122320-73-4, BRL-49653 167869-21-8, PD98059
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)
IT 56-81-5, 1,2,3-Propanetriol, biological studies 9001-62-1 137632-07-6, ERK1 kinase 137632-08-7, ERK2 kinase 142243-02-5, MAP kinase 142805-58-1, MAP kinase kinase 155215-87-5, **JNK** kinase 165245-96-5, p38 Kinase 169494-85-3, Leptin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)
IT 9004-10-8, Insulin, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(resistance; MAPK/ERK, **JNK**, or p38 signal transduction pathway modulator for treatment of disorders associated with TNF-α-induced lipolysis)

L6 ANSWER 11 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:686849 CAPLUS
DN 132:220318
TI Role of MAP kinases in shock caused by bacterial **endotoxin**
AU Kato, Yutaka; Yokochi, Takashi
CS Biol. Immunol. Intract. Dis. Res. Cent., Aichi Med. Univ., Japan
SO Gendai Igaku (**1999**), 47(1), 163-169
CODEN: GEIGAI; ISSN: 0433-3047
PB Aichi-ken Ishikai
DT Journal; General Review
LA Japanese
TI Role of MAP kinases in shock caused by bacterial **endotoxin**
SO Gendai Igaku (**1999**), 47(1), 163-169
CODEN: GEIGAI; ISSN: 0433-3047
AB A review with 43 refs. Lipopolysaccharide (LPS) activate many signal transducing mols. in macrophage including MAP kinase in **endotoxin** shock. The possible participation of MAP kinase family and related factors (protein p38, ERK kinase, **JNK** kinase, and BMK1 kinase) in **endotoxin** shock are discussed.
ST review MAP kinase bacterial **endotoxin** shock
IT Shock (circulatory collapse)
(septic; MAP kinases in shock caused by bacterial **endotoxin**)
IT 142243-02-5, Map kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MAP kinases in shock caused by bacterial **endotoxin**)

L6 ANSWER 12 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:632070 CAPLUS
DN 131:332518
TI Angiotensin II stimulates platelet-derived growth factor-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, extracellular signal-regulated protein kinase, and c-Jun N-terminal protein kinase mechanisms
AU Deguchi, Jun-O.; Makuuchi, Masatoshi; Nakaoka, Takashi; Collins, Tucker; Takuwa, Yoh

CS Departments of Molecular and Cellular Physiology, Graduate School of Medicine, University of Tokyo, Japan
SO Circulation Research (**1999**), 85(7), 565-574
CODEN: CIRUAL; ISSN: 0009-7330
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Circulation Research (**1999**), 85(7), 565-574
CODEN: CIRUAL; ISSN: 0009-7330
AB Platelet-derived growth factors (PDGFs) have been implicated in the pathogenesis of vascular proliferative disorders. Vascular smooth muscle cells (VSMCs) are one of the cell types that produce PDGF-B chain in proliferative lesions, although the mechanism of regulation of PDGF-B chain production in these cells is not well understood. In the present study, we demonstrate that angiotensin II (Ang II), which is also implicated in vascular stenosis after **angioplasty** and **atherosclerosis**, markedly stimulates PDGF-B chain mRNA expression in cultured newborn rat medial VSMCs and neointimal VSMCs via an AT1, but not in adult rat VSMCs. In newborn rat VSMCs, Ang II activates extracellular signal-regulated protein kinase (ERK), c-Jun N-terminal protein kinase (**JNK**), and p38 mitogen-activated protein kinase. The mitogen-activated protein/ERK (MEK) inhibitor PD98059, but not the p38 inhibitor SB203580, abrogates Ang II-induced PDGF-B mRNA expression. Transient transfection anal. using a PDGF-B promoter-luciferase gene reporter construct reveals that Ang II induces transcriptional activation of PDGF-B chain gene, which is abolished by the expression of a dominant neg. form of either ERK or **JNK**, but not of p38. The expression of a dominant neg. form of Ras abolishes the stimulatory effects of Ang II on ERK activity and PDGF-B mRNA expression. In adult rat VSMCs, Ang II activates ERK and **JNK**, but weakly induces Egr-1, a transcription factor implicated in PDGF-B chain gene expression, compared with newborn VSMCs. These data indicate that Ang II activates PDGF-B chain gene expression in VSMCs through mechanisms involving Ras-ERK and **JNK**.
IT Angiotensin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AT1; angiotensin II stimulates PDGF-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, ERK, and **JNK** mechanisms)
IT Platelet-derived growth factors
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(B-chain; angiotensin II stimulates PDGF-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, ERK, and **JNK** mechanisms)
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Egr-1; angiotensin II stimulates PDGF-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, ERK, and **JNK** mechanisms)
IT Newborn
Signal transduction, biological
(angiotensin II stimulates PDGF-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, ERK, and **JNK** mechanisms)
IT Ras proteins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);

PROC (Process)
(angiotensin II stimulates PDGF-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, ERK, and **JNK** mechanisms)

IT Blood vessel
(smooth muscle; angiotensin II stimulates PDGF-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, ERK, and **JNK** mechanisms)

IT 142243-02-5, Extracellular signal-regulated protein kinase 155215-87-5
165245-96-5, p38 Mitogen-activated protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(angiotensin II stimulates PDGF-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, ERK, and **JNK** mechanisms)

IT 11128-99-7, Angiotensin II
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(angiotensin II stimulates PDGF-B chain expression in newborn rat vascular smooth muscle cells and neointimal cells through Ras, ERK, and **JNK** mechanisms)

L6 ANSWER 13 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:568518 CAPLUS
DN 131:281965
TI Extracellular signal-regulated protein kinase activation is required for the anti-hypertrophic effect of atrial natriuretic factor in neonatal rat ventricular myocytes
AU Silberbach, Michael; Gorenc, Travis; Hershberger, Ray E.; Stork, Philip J. S.; Steyger, Peter S.; Roberts, Charles T., Jr.
CS Department of Pediatrics, Oregon Health Sciences University, Portland, OR, 97201, USA
SO Journal of Biological Chemistry (**1999**), 274(35), 24858-24864
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Biological Chemistry (**1999**), 274(35), 24858-24864
CODEN: JBCHA3; ISSN: 0021-9258
AB Atrial natriuretic factor (ANF) inhibits proliferation in non-myocardial cells and is thought to be anti-hypertrophic in cardiomyocytes. The authors investigated the possibility that the anti-hypertrophic actions of ANF involved the mitogen-activated protein kinase signal transduction cascade. Cultured neonatal rat ventricular myocytes treated for 48 h with the α1-adrenergic agonist phenylephrine (PE) had an 80% increase in cross-sectional area (CSA). ANF alone had no effect but inhibited PE-induced increases in CSA by approx. 50%. The mitogen-activated protein kinase/ERK kinase (MEK) inhibitor PD098059 minimally inhibited PE-induced increases in CSA, but it completely abolished ANF-induced inhibition of PE-induced increases. ANF-induced extracellular signal-regulated protein kinase (ERK) nuclear translocation was also eliminated by PD098059. ANF treatment caused MEK phosphorylation and activation but failed to activate any of the Raf isoforms. ANF induced a rapid increase in ERK phosphorylation and in vitro kinase activity. PE also increased ERK activity, and the combined effect of ANF and PE appeared to be additive. ANF-induced ERK phosphorylation was eliminated by PD098059. ANF induced minimal phosphorylation of **JNK** or p38, indicating that its effect on ERK was specific. ANF-induced activation of ERK was mimicked by cGMP analogs, suggesting that ANF-induced ERK activation involves the

guanylyl cyclase activity of the ANF receptor. These data suggest that there is an important linkage between cGMP signaling and the mitogen-activated protein kinase cascade and that selective ANF activation of ERK is required for the anti-hypertrophic action of ANF. Thus, ANF expression might function as the natural defense of the heart against maladaptive **hypertrophy** through its ability to activate ERK.

IT Heart, disease
(ventricle, **hypertrophy**; extracellular signal-regulated protein kinase signaling pathway involvement in anti-hypertrophic effect of atrial natriuretic factor in neonatal rat ventricular myocytes)

L6 ANSWER 14 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:562535 CAPLUS
DN 131:270462
TI MAPK activation determines renal epithelial cell survival during oxidative injury
AU Di Mari, John F.; Davis, Roger; Safirstein, Robert L.
CS University of Texas Medical Branch at Galveston, Galveston, TX, 77555-0562, USA
SO American Journal of Physiology (**1999**), 277(2, Pt. 2), F195-F203
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO American Journal of Physiology (**1999**), 277(2, Pt. 2), F195-F203
CODEN: AJPHAP; ISSN: 0002-9513
AB **Ischemia**/reperfusion (I/R) injury induces both functional and morphol. changes in the kidney. Necrosis, predominantly of the proximal tubule (PT), is the hallmark of this model of renal injury, whereas cells of the distal nephron survive, apparently intact. The authors examined whether differences in cellular outcome of the various regions of the nephron may be due to segmental variation in the activation of the mitogen-activated protein kinases (MAPKs) in response to I/R injury. Whereas c-Jun N-terminal kinase (**JNK**) is activated in both the cortex and inner stripe of the outer medulla, the extracellular regulated kinase (ERK) pathway is activated only in the inner stripe in which thick ascending limb (TAL) cells predominate. These studies are consistent with the notion that ERK activation is essential for survival. To test this hypothesis directly, the authors studied an in vitro system in which manipulation of these pathways and their effects on cellular survival could be examined Oxidant injury was induced in mouse PT and TAL cells in culture by the catabolism of hypoxanthine by xanthine oxidase. PT cells were more sensitive than TAL cells to oxidative stress as assessed by cell counting, light microscopy, propidium iodide uptake, and fluorescence-activated cell sorting (FACS) anal. Immunopptn./kinase anal. revealed that **JNK** activation occurred in both cell types, whereas ERK activation occurred only in TAL cells. The authors then examined the effect of PD-098059, a MAP kinase kinase (MEK)-1 inhibitor of the ERK pathway, on PT and TAL survival. In TAL cells, ERK inhibition reduced cell survival nearly fourfold after oxidant exposure. In PT cells, activation of the ERK pathway by insulin-like growth factor I (IGF-I) increased survival by threefold, and this IGF-I-enhanced cell survival was inhibited by PD-098059. These results indicate that cell survival in the kidney after **ischemia** may be dependent on ERK activation, suggesting that this pathway may be a target for therapeutic treatment in I/R injury.

IT Kidney, disease
(**ischemia**; MAPK activation dets. renal epithelial cell survival during oxidative injury)

L6 ANSWER 15 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:558046 CAPLUS
DN 131:309458
TI Lysophosphatidylcholine phosphorylates CREB and activates the jun2TRE site of c-jun promoter in vascular endothelial cells
AU Ueno, Y.; Kume, N.; Miyamoto, S.; Morimoto, M.; Kataoka, H.; Ochi, H.; Nishi, E.; Moriwaki, H.; Minami, M.; Hashimoto, N.; Kita, T.
CS Graduate School of Medicine, Department of Neurosurgery, Kyoto University, Kyoto, Japan
SO FEBS Letters (**1999**), 457(2), 241-245
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO FEBS Letters (**1999**), 457(2), 241-245
CODEN: FEBLAL; ISSN: 0014-5793
AB Lysophosphatidylcholine (lyso-PC), a polar phospholipid increased in atherogenic lipoproteins and atherosclerotic lesions, has been shown to induce transcription of a variety of endothelial genes relevant to atherogenesis. Lyso-PC has been shown to activate c-jun N-terminal kinase (**JNK**) and activator protein 1 (AP-1) and thereby stimulate transcription of the c-jun gene. Here, we provide evidence that lyso-PC can phosphorylate cAMP-responsive element-binding protein (CREB) and thereby activate the jun2 12-O-tetradecanoylphorbol 13-acetate-response element (jun2TRE) site of the c-jun promoter, which appears to be the major mol. mechanism involved in lyso-PC-induced c-jun gene expression in cultured bovine aortic endothelial cells (BAEC). Transient transfection of BAEC with a 1.6-kbp c-jun promoter and luciferase reporter fusion gene resulted in a 12.9-fold increase in luciferase activity by lyso-PC treatment. Serial deletion mutation in the c-jun promoter and luciferase reporter gene assay revealed that the 5' promoter region between nucleotide nos. -268 and -127, which contains a jun2TRE binding sequence, was most crucial for lyso-PC-induced transcription. The 5' promoter region between -76 and -27, which contains an AP-1 site, also affected lyso-PC-induced transcription of the c-jun gene. Point mutation in the jun2TRE site reduced lyso-PC-induced transcription of the c-jun promoter-luciferase fusion gene by a 70.3% decrease in c-jun promoter activity. Electrophoretic mobility shift assays showed increased binding of 32P-labeled oligonucleotides with jun2TRE in nuclear exts. isolated from lyso-PC-treated BAEC, which was abolished or supershifted by anti-CREB antibody. Immunoblotting with anti-phosphorylated CREB antibody showed rapid phosphorylation of this protein after lyso-PC treatment. These results indicate that lyso-PC phosphorylates CREB, which was then bound to the jun2TRE site of the c-jun promoter and activated transcription. Activation of jun2TRE may play a key role in the transcriptional activation of c-jun as well as other endothelial genes depending upon these transcription factors.
ST lysophosphatidylcholine phosphorylation CREB activation jun2TRE site promoter cjun gene; vascular endothelium c jun gene transcription activation lysoPC **atherosclerosis**
IT **Atherosclerosis**
Inflammation
(lyso-PC in relation to; lysophosphatidylcholine (lyso-PC) phosphorylates CREB and activates jun2TRE site of c-jun promoter in vascular endothelial cells)

L6 ANSWER 16 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:514352 CAPLUS
DN 131:270833

TI Unresponsiveness of MyD88-deficient mice to **endotoxin**
AU Kawai, Taro; Adachi, Osamu; Ogawa, Tomohiko; Takeda, Kiyoshi; Akira, Shizuo
CS Department of Biochemistry, Hyogo College of Medicine, Japan Science and Technology Corporation, Hyogo, 663-8501, Japan
SO Immunity (**1999**), 11(1), 115-122
CODEN: IUNIEH; ISSN: 1074-7613
PB Cell Press
DT Journal
LA English
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Unresponsiveness of MyD88-deficient mice to **endotoxin**
SO Immunity (**1999**), 11(1), 115-122
CODEN: IUNIEH; ISSN: 1074-7613
ST MyD88 deficient mouse **endotoxin** unresponsiveness
IT Cell proliferation
(B cell; unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to)
IT Mouse
(MyD88; unresponsiveness of MyD88-deficient mice to **endotoxin**)
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-κB (nuclear factor κB); unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to activation of)
IT Lipopolysaccharides
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(bacterial; unresponsiveness of MyD88-deficient mice to **endotoxin**)
IT Fibroblast
(embryonic; unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to cytokine secretion by)
IT Toxins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endotoxins; unresponsiveness of MyD88-deficient mice to **endotoxin**)
IT Embryo, animal
(fibroblast; unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to cytokine secretion by)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene MyD88; unresponsiveness of MyD88-deficient mice to **endotoxin**)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene Toll; unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to)
IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inflammatory; unresponsiveness of MyD88-deficient mice to **endotoxin** but no changes in)
IT Cell activation

(macrophage; unresponsiveness of MyD88-deficient mice to **endotoxin** but no changes in)
IT Shock (circulatory collapse)
(septic; unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to)
IT Interleukin 1 receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type I; unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to activation of)
IT B cell (lymphocyte)
(unresponsiveness of MyD88-deficient mice to **endotoxin** but no changes in)
IT Signal transduction, biological
(unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to)
IT Interleukin 1 receptors
Interleukin 18
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to)
IT Macrophage
(unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to cytokine secretion by)
IT 142243-02-5, Map kinase 155215-87-5, **Jnk** kinase 167397-96-8, Irak kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(unresponsiveness of MyD88-deficient mice to **endotoxin** in relation to activation of)

L6 ANSWER 17 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:506564 CAPLUS
DN 132:21323
TI ATF3 and stress responses
AU Hai, Tsonwin; Wolfgang, Curt D.; Marsee, Derek K.; Allen, Amy E.; Sivaprasad, Umasundari
CS Department of Medical Biochemistry, Neurobiotechnology Center, Ohio State Biochemistry Program, Ohio State University, Columbus, OH, 43210, USA
SO Gene Expression (**1999**), 7(4-5-6), 321-335
CODEN: GEEXEJ; ISSN: 1052-2166
PB Cognizant Communication Corp.
DT Journal; General Review
LA English
RE.CNT 144 THERE ARE 144 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Gene Expression (**1999**), 7(4-5-6), 321-335
CODEN: GEEXEJ; ISSN: 1052-2166
AB A review with 144 refs. The purpose of this review is to discuss ATF3, a member of the ATF/CREB family of transcription factors, and its roles in stress responses. In the introduction, we briefly describe the ATF/CREB family, which contains more than 10 proteins with the basic region-leucine zipper (bZip) DNA binding domain. We summarize their DNA binding and heterodimer formation with other bZip proteins, and discuss the nomenclature of these proteins. Over the years, identical or homologous cDNA clones have been isolated by different labs. and given different names. We group these proteins into subgroups according to their amino acid similarity; we also list the alternative names for each member, and clarify some potential confusion in the nomenclature of this family of proteins. We then focus on ATF3 and its potential roles in stress responses. We review the evidence that the mRNA level of ATF3 greatly

increases when the cells are exposed to stress signals. In animal expts., the signals include **ischemia**, **ischemia** coupled with reperfusion, wounding, axotomy, toxicity, and seizure; in cultured cells, the signals include serum factors, cytokines, genotoxic agents, cell death-inducing agents, and the adenoviral protein E1A. Despite the overwhelming evidence for its induction by stress signals, not much else is known about ATF3. Preliminary results suggest that the **JNK** /SAPK pathway is involved in the induction of ATF3 by stress signals; in addition, IL-6 and p53 have been demonstrated to be required for the induction of ATF3 under certain conditions. The consequences of inducing ATF3 during stress responses are not clear. Transient transfection and in vitro transcription assays indicate that ATF3 represses transcription as a homodimer; however, ATF3 can activate transcription when coexpressed with its heterodimeric partners or other proteins. Therefore, it is possible that, when induced during stress responses, ATF3 activates some target genes but represses others, depending on the promoter context and cellular context. Even less is understood about the physiol. significance of inducing ATF3. We will discuss our preliminary results and some reports by other investigators in this regard.

L6 ANSWER 18 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:489052 CAPLUS
DN 131:252314
TI Okadaic acid and anisomycin are protective and stimulate the SAPK/**JNK** pathway
AU Barancik, Miroslav; Htun, Patrik; Schaper, Wolfgang
CS Department of Experimental Cardiology, Max-Planck-Institute for Physiological and Clinical Research, Bad Nauheim, D-61231, Germany
SO Journal of Cardiovascular Pharmacology (**1999**), 34(2), 182-190
CODEN: JCPCDT; ISSN: 0160-2446
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Okadaic acid and anisomycin are protective and stimulate the SAPK/**JNK** pathway
SO Journal of Cardiovascular Pharmacology (**1999**), 34(2), 182-190
CODEN: JCPCDT; ISSN: 0160-2446
AB We report that okadaic acid (OA), a known inhibitor of Ser/Thr phosphatases, protects pig myocardium against **ischemic** injury in an in vivo model and stimulates the activities of stress-activated protein kinases/c-Jun N-terminal kinases (SAPKs/JNKs). When OA was directly infused into the subsequently **ischemic** myocardium for 60 min before a 60-min period of coronary occlusion followed by reperfusion, infarct size was reduced from a control value of 83.4±2.8% of the risk region to 40.7±9.1%. When OA was infused for 10 min before a 5-min occlusion and during 45 min thereafter, infarct size was reduced to 26.5%. In a sep. set of similar expts., we pretreated pig hearts in vivo with the protein-synthesis inhibitor and known activator of SAPK/**JNK**, anisomycin (AN), and found that this compound also significantly reduced infarct size from 83.4±2.8.1% to 48.1±5.1%. For in vitro assays, OA (600 nM), AN (500 μM), or solvent (KHB) were locally infused into the left ventricular myocardium, and biopsies from in situ beating hearts were obtained after 10, 30, and 60 min of infusion. The activities of Ser/Thr phosphatases (PPases), especially PP-2A, were significantly decreased after OA infusion. OA infusion increased the activity (in-gel phosphorylation of N-terminal c-Jun1-135) of both 46- and 55-kDa SAPK/JNKs (twofold to threefold, 30 and 60 min of infusion), and this increase correlated well with the observed decrease of PPase activities. Western blot anal. with a phospho-specific SAPK/**JNK** (Thr 183/Tyr 185) antibody showed an increased content of the phosphorylated forms after OA treatment. We

observed significant stimulation of SAPK/**JNK** activity also after AN treatment (threefold to fourfold, after 30 min of infusion). In contrast to the SAPK/JNKs, the infusion of both OA and AN did not significantly change the activities and phosphorylation of extracellular signal-related kinases (ERKs) and p38-MAPK. The findings that the protective effect of both OA and AN correlates with increased activity of SAPK/JNKs suggest the involvement of these enzymes in the mechanism of cardioprotection.

IT Cytoprotective agents
(cardioprotective; okadaic acid and anisomycin are cardioprotective and stimulate the SAPK/**JNK** pathway)

IT Heart, disease
(**ischemia**; okadaic acid and anisomycin are cardioprotective and stimulate the SAPK/**JNK** pathway)

IT Reperfusion
(okadaic acid and anisomycin are cardioprotective and stimulate the SAPK/**JNK** pathway)

IT 22862-76-6, Anisomycin 78111-17-8, Okadaic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(okadaic acid and anisomycin are cardioprotective and stimulate the SAPK/**JNK** pathway)

IT 9025-73-4, Serine phosphatase 142243-02-5, MAP kinase 155215-87-5, c-Jun N-terminal kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(okadaic acid and anisomycin are cardioprotective and stimulate the SAPK/**JNK** pathway)

L6 ANSWER 19 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:486610 CAPLUS
DN 131:256139
TI Lipopolysaccharide-induced tumor necrosis factor alpha production by human monocytes involves the Raf-1/MEK1-MEK2/ERK1-ERK2 pathway
AU Van der Bruggen, Tjomme; Nijenhuis, Suzanne; Van Raaij, Estia; Verhoef, Jan; Van Asbeck, B. Sweder
CS Eijkman-Winkler Institute for Microbiology, Infectious Diseases and Inflammation, Utrecht, Neth.
SO Infection and Immunity (**1999**), 67(8), 3824-3829
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Infection and Immunity (**1999**), 67(8), 3824-3829
CODEN: INFIBR; ISSN: 0019-9567
AB During gram-neg. sepsis, human monocytes are triggered to produce large quantities of proinflammatory cytokines such as tumor necrosis factor α (TNF-α) in response to **endotoxin** [lipopolysaccharide (LPS)]. Several studies have identified signal transduction pathways that are activated by LPS, including activation of nuclear factor-κB (NF-κB) and activation of mitogen-activated protein kinases (MAPKs), including ERK1 and ERK2, c-Jun N-terminal kinase, and p38. Here, the relevance of ERK1 and ERK2 activation for LPS-induced TNF-α production by primary human monocytes has been addressed with PD-098059, which specifically blocks activation of MAPK kinase (MEK) by Raf-1. TNF-α levels in the monocyte culture supernatant, induced by 10 ng of LPS/mL, were reduced by PD-098059 (50 μM). In addition, PD-098059 also reduced TNF-α mRNA expression when cells were stimulated for 1 h with LPS. LPS-induced interleukin-10 (IL-10) levels in the monocyte supernatant were only slightly inhibited by PD-098059. Ro

09-2210, a recently identified MEK inhibitor, completely abrogated TNF-α levels at nanomolar concns. IL-10 levels also were strongly reduced. To show the efficacy of PD-098059 and Ro 09-2210, ERK1 and -2 activation was monitored by Western blotting with an antiserum that recognizes the phosphorylated (i.e., activated) forms of ERK1 and ERK2. Addition of LPS to human monocytes resulted in activation of both ERK1 and ERK2 in a time- and concentration (50% effective concentration between 1 and 10 ng of LPS/mL)-dependent manner. Activation of ERK2 was blocked by PD-098059 (50 μM), whereas ERK1 seemed to be less affected. Ro 09-2210 completely prevented LPS-induced ERK1 and ERK2 activation. LPS-induced p38 activation also was prevented by Ro 09-2210. Thus, the ERK signal transduction pathway is causally involved in the synthesis of TNF-α by human monocytes stimulated with LPS.

IT 137632-07-6, ERK1 kinase 137632-08-7, ERK2 kinase 139691-76-2, Raf-1 kinase 142805-58-1, MEK-1 kinase 150316-14-6, MEK2 kinase 155215-87-5, **Jnk** kinase 165245-96-5, p38 Kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(lipopolysaccharide-induced tumor necrosis factor α formation by human monocytes involves Raf-1/MEK1-MEK2/ERK1-ERK2 pathway)

L6 ANSWER 20 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:473436 CAPLUS
DN 131:284592
TI Apoptosis in myocardial **ischemia**-reperfusion
AU Gottlieb, Roberta A.; Engler, Robert L.
CS Division of Biochemistry, Department of Molecular & Experimental Medicine, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Annals of the New York Academy of Sciences (**1999**), 874(Heart in Stress), 412-426
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal; General Review
LA English
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Apoptosis in myocardial **ischemia**-reperfusion
SO Annals of the New York Academy of Sciences (**1999**), 874(Heart in Stress), 412-426
CODEN: ANYAA9; ISSN: 0077-8923
AB A review, with 56 refs. The signal transduction pathways by which **ischemia**-reperfusion leads to apoptosis may involve the **JNK** pathway, ceramide generation, and inhibition of protective PKC pathways. The biochem. events associated with apoptosis include mitochondrial inactivation, cytochrome c dislocation, caspase activation, and cytoplasmic acidification. Through the concerted efforts of multiple classes of enzymes, apoptosis is accomplished, resulting in the death of a cell in which potentially transforming oncogenes have been degraded and inflammatory contents are contained within the plasma membrane until the fragments can be ingested by phagocytes. This non-inflammatory mode of cell death permits tissue remodeling with minimal scar formation, and so is preferable to necrotic cell death. The distinction between apoptosis and necrosis, which implies different mechanisms of cell death, is blurred in the case of a pathol. insult such as **ischemia**-reperfusion. It is suggested that it is more useful to view cell death in the context of whether or not it can be prevented.
ST review myocardial **ischemia** reperfusion apoptosis
IT Apoptosis
Signal transduction, biological
(biochem. mechanisms of signaling leading to apoptosis in myocardial

ischemia-reperfusion)
IT Reperfusion
(injury; biochem. mechanisms of signaling leading to apoptosis in myocardial **ischemia**-reperfusion)
IT Heart, disease
(**ischemia**; biochem. mechanisms of signaling leading to apoptosis in myocardial **ischemia**-reperfusion)

L6 ANSWER 21 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:467617 CAPLUS
DN 131:240970
TI Activation and expression of ERK, **JNK**, and p38 MAP-kinases in isolated islets of Langerhans: implications for cultured islet survival
AU Paraskevas, Steven; Aikin, Reid; Maysinger, Dusica; Lakey, Jonathan R. T.; Cavanagh, Thomas J.; Hering, Bernhard; Wang, Rennian; Rosenberg, Lawrence
CS Department of Surgery, The Montreal General Hospital, Montreal, QC, Can.
SO FEBS Letters (**1999**), 455(3), 203-208
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Activation and expression of ERK, **JNK**, and p38 MAP-kinases in isolated islets of Langerhans: implications for cultured islet survival
SO FEBS Letters (**1999**), 455(3), 203-208
CODEN: FEBLAL; ISSN: 0014-5793
AB Isolation and purification of islet cells exposes them to **ischemic**, osmotic, and mech. stresses. The objective of this study was to determine the roles of the MAP kinases in islets immediately following isolation. During the 1st 48 h, activity of JNK1 and JNK2 declined markedly. Activity of p38 increased steadily with time in culture while extracellular signal regulated kinase (ERK) activity declined dramatically within 24 h post-isolation. High p38 activation relative to ERK activation immediately following isolation correlated with a decrease in islet survival after 36 h in culture. Absence and/or transiency of ERK signaling in conjunction with sustained activation of p38 pathway could be an important regulator of cell death in islets during and following their isolation by commonly employed procedures.
IT Apoptosis
Dog (Canis familiaris)
Pancreatic islet of Langerhans
Swine
(activation and expression of ERK, **JNK**, and p38 MAP-kinases in isolated islets of Langerhans of humans and other animals)
IT Animal tissue culture
(mammalian; activation and expression of ERK, **JNK**, and p38 MAP-kinases in isolated islets of Langerhans of humans and other animals)
IT Phosphorylation, biological
(protein; activation and expression of ERK, **JNK**, and p38 MAP-kinases in isolated islets of Langerhans of humans and other animals)
IT 137632-07-6, ERK1 kinase 137632-08-7, ERK2 kinase 137632-08-7
150605-50-8, MAP kinase phosphatase-1 155215-87-5, JNK1 kinase
165245-96-5, p38 MAP kinase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(activation and expression of ERK, **JNK**, and p38 MAP-kinases in isolated islets of Langerhans of humans and other animals)

L6 ANSWER 22 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:467598 CAPLUS
DN 131:238103
TI Differential effects of 17β-estradiol on mitogen-activated protein kinase pathways in rat cardiomyocytes
AU Nuedling, Simone; Kahlert, Stefan; Loebbert, Kerstin; Meyer, Rainer; Vetter, Hans; Grohe, Christian
CS Medizinische Poliklinik, University of Bonn, Bonn, 53111, Germany
SO FEBS Letters (**1999**), 454(3), 271-276
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO FEBS Letters (**1999**), 454(3), 271-276
CODEN: FEBLAL; ISSN: 0014-5793
AB Cardiac myocytes contain functional estrogen receptors, however, the effect of estrogen on growth-related signaling pathways such as mitogen-activated protein kinases (MAPK) in the pathogenesis of cardiac disease is unclear. MAPKs are critically involved in regulatory signaling pathways which ultimately lead to cardiac **hypertrophy**. Here we show that 17β-estradiol (E2) activates extracellular signal-regulated kinase (ERK1/2), c-Jun-NH2-terminal protein kinase (**JNK**) and p38 in rat cardiomyocytes in a distinctive pattern. As shown by immunoblot anal. and phosphorylation assays, E2 (10-9 M) induced a rapid and transient activation of ERK1/2 and a rapid but sustained increase of **JNK** phosphorylation. In contrast, E2 had only a marginal effect on p38 activation. Furthermore, MAPK phosphatase expression was induced by E2 and E2-stimulated expression of endothelial and inducible NO synthase was inhibited by PD 98059, an inhibitor of the ERK pathway. These novel observations may help to explain the role of estrogen in gender-based differences found in cardiac disease.

L6 ANSWER 23 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:465421 CAPLUS
DN 131:255714
TI Activation of c-Jun N-Terminal Kinases and p38-Mitogen-activated Protein Kinases in Human Heart Failure Secondary to **Ischemic** Heart Disease
AU Cook, Stuart A.; Sugden, Peter H.; Clerk, Angela
CS NHLI Division (Cardiac Medicine), Imperial College School of Medicine, London, UK
SO Journal of Molecular and Cellular Cardiology (**1999**), 31(8), 1429-1434
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic Press
DT Journal
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Activation of c-Jun N-Terminal Kinases and p38-Mitogen-activated Protein Kinases in Human Heart Failure Secondary to **Ischemic** Heart Disease
SO Journal of Molecular and Cellular Cardiology (**1999**), 31(8), 1429-1434
CODEN: JMCDAY; ISSN: 0022-2828
AB Three well-characterized mitogen-activated protein kinase (MAPK) subfamilies are expressed in rodent and rabbit hearts, and are activated by pathophysiol. stimuli. We have determined and compared the expression and activation of these MAPKs in donor and failing human hearts. The amount and activation of MAPKs was assessed in samples from the left ventricles of 4

unused donor hearts and 12 explanted hearts from patients with heart failure secondary to **ischemic** heart disease. Total MAPKs or dually phosphorylated (activated) MAPKs were detected by Western blotting and MAPK activities were measured by in gel kinase assays. As in rat heart, c-Jun N-terminal kinases (JNKs) were detected in human hearts as bands corresponding to 46 and 54 kDa; p38-MAPK(s) was detected as a band corresponding to approx. 40 kDa, and extracellularly regulated kinases, ERK1 and ERK2, were detected as 44- and 42-kDa bands resp. The total amts. of 54 kDa **JNK**, p38-MAPK and ERK2 were similar in all samples, although 46-kDa **JNK** was reduced in the failing hearts. However, the mean activities of JNKs and p38-MAPK(s) were significantly higher in failing heart samples than in those from donor hearts. There was no significant difference in phosphorylated (activated) ERKs between the two groups. In conclusion, JNKs, p38-MAPK(s) and ERKs are expressed in the human heart and the activities of JNKs and p38-MAPK(s) were increased in heart failure secondary to **ischemic** heart disease. These data indicate that JNKs and p38-MAPKs may be important in human cardiac pathol. (c) 1999 Academic Press.

ST heart failure **ischemia JNK** p38 MAP kinase

IT Heart, disease
(failure; activation of c-jun N-terminal kinases and p38-mitogen-activated protein kinases in human heart failure secondary to **ischemic** heart disease)

IT Heart, disease
(**ischemia**; activation of c-jun N-terminal kinases and p38-mitogen-activated protein kinases in human heart failure secondary to **ischemic** heart disease)

IT Heart
(left ventricle; activation of c-jun N-terminal kinases and p38-mitogen-activated protein kinases in human heart failure secondary to **ischemic** heart disease)

IT 155215-87-5, c-Jun N-Terminal kinase 165245-96-5, p38-Mitogen-activated protein kinase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(activation of c-jun N-terminal kinases and p38-mitogen-activated protein kinases in human heart failure secondary to **ischemic** heart disease)

IT 137632-07-6, ERK 1 kinase 137632-08-7, ERK 2 kinase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(in human heart failure secondary to **ischemic** heart disease)

IT 137632-07-6 137632-08-7
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(in human heart failure secondary to **ischemic** heart disease)

L6 ANSWER 24 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:443367 CAPLUS
DN 131:227337
TI CD4-mediated signals induce T cell dysfunction in vivo
AU Chirmule, Narendra; Avots, Andris; LakshmiTamma, S. M.; Pahwa, Savita; Serfling, Edgar
CS Institute for Human Gene Therapy, University of Pennsylvania, Philadelphia, PA, 19104, USA
SO Journal of Immunology (**1999**), 163(2), 644-649
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Journal of Immunology (**1999**), 163(2), 644-649
CODEN: JOIMA3; ISSN: 0022-1767

AB Triggering of CD4 coreceptors on both human and murine T cells can suppress TCR/CD3-induced secretion of IL-2. The authors show here that pretreatment of murine CD4+ T cells with the CD4-specific mAb YTS177 inhibits the CD3-mediated activation of the IL-2 promoter factors NF-AT and AP-1. Ligation of CD4 mols. on T cells leads to a transient stimulation of extracellular signal-regulated kinase (Erk) 2, but not c-Jun N-terminal kinase (**JNK**) activity. Pretreatment with anti-CD4 mAb impaired anti-CD3-induced Erk2 activation. Costimulation with anti-CD28 overcame the inhibitory effect of anti-CD4 Abs, by induction of **JNK** activation. The in vivo relevance of these studies was demonstrated by the observation that CD4+ T cells from BALB/c mice injected with non-depleting anti-CD4 mAb were inhibited in their ability to respond to OVA Ag-induced proliferation and IL-3 secretion. Interestingly, in vivo stimulation with anti-CD28 mAb restored IL-2 secretion. Furthermore, animals pretreated with anti-CD4 elicited enhanced IL-4 secretion induced by OVA and CD28. These observations suggest that CD4-specific Abs can inhibit T cell activation by interfering with signal 1 transduced through the TCR, but potentiate those delivered through the costimulatory mol. CD28. These studies have relevance to understanding the mechanism of tolerance induced by non-depleting anti-CD4 mAb used in animal models for allograft studies, autoimmune pathologies, and for immunosuppressive therapies in humans.

IT **Transplant** rejection
(allotransplant; CD4-mediated signals induce T cell dysfunction in relation to)

L6 ANSWER 25 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:437882 CAPLUS
DN 131:194747
TI Leptin induces oxidative stress in human endothelial cells
AU Bouloumie, Anne; Marumo, Takeshi; Lafontan, Max; Busse, Rudi
CS Institut fur Kardiovaskulare Physiologie, Klinikum der J. W. Goethe-Universitat, Frankfurt/Main, 60590, Germany
SO FASEB Journal (**1999**), 13(10), 1231-1238
CODEN: FAJOEC; ISSN: 0892-6638
PB Federation of American Societies for Experimental Biology
DT Journal
LA English

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO FASEB Journal (**1999**), 13(10), 1231-1238
CODEN: FAJOEC; ISSN: 0892-6638

AB Human umbilical vein endothelial cells (HUVEC) express functional receptors to leptin, the product of the ob gene. As human obesity is associated with **atherosclerosis** and hyperleptinemia, we investigated whether leptin, in addition to its angiogenic properties, exerts atherogenic effects through the generation of oxidative stress in endothelial cells. In HUVEC leptin increased the accumulation of reactive oxygen species (ROS), as assessed by the oxidation of 2',7'-dichlorodihydrofluorescein, in a time- and concentration-dependent manner. In addition, leptin activated the NH2-terminal c-Jun kinase/stress-activated protein kinase pathway as demonstrated by enhanced **JNK** activity and AP-1 DNA binding. Both effects were sensitive to antioxidant treatment with N-acetylcysteine. NF-κB, another redox-sensitive transcription factor, was also activated by leptin stimulation in an oxidant-dependent manner. Finally, activation of both AP-1 and NF-κB was associated with an enhanced expression of the monocyte chemoattractant protein-1 in HUVEC. These findings demonstrate that ROS

are second messengers involved in leptin-induced signaling in endothelial cells. Thus, chronic oxidative stress in endothelial cells under hyperleptinemia may activate atherogenic processes and contribute to the development of vascular pathol.

ST leptin oxidative stress vascular endothelium; **atherosclerosis** leptin transcription factor

IT **Atherosclerosis**
Obesity
Oxidative stress, biological
Second messenger system
(leptin induces oxidative stress in human endothelial cells)

L6 ANSWER 26 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:394116 CAPLUS
DN 131:183837
TI Lipopolysaccharide tolerance in murine peritoneal macrophages induces downregulation of the lipopolysaccharide signal transduction pathway through mitogen-activated protein kinase and nuclear factor-κB cascades, but not lipopolysaccharide-incorporation steps
AU Tominaga, Kaoru; Saito, Shinji; Matsuura, Motohiro; Nakano, Masayasu
CS Department of Microbiology, Jichi Medical School, Tochigi-ken, Japan
SO Biochimica et Biophysica Acta (**1999**), 1450(2), 130-144
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Biochimica et Biophysica Acta (**1999**), 1450(2), 130-144
CODEN: BBACAQ; ISSN: 0006-3002
AB **Endotoxin**/lipopolysaccharide (LPS) tolerance, a hyporesponsive state to **endotoxin** or LPS stimulation, was induced in murine peritoneal macrophages by previous exposure of macrophages to LPS. Expression of tumor necrosis factor (TNF)-α and interleukin (IL)-6 mRNA in response to LPS stimulation was suppressed in LPS-tolerant macrophages. Tyrosine phosphorylations in response to LPS of 40-45-kDa proteins in non-tolerant macrophages were also suppressed in LPS-tolerant macrophages. These proteins corresponded to two members of the mitogen-activated protein kinase (MAPK) family, ERK and p38. In addition to these proteins, another MAPK family protein, **JNK**, was also suppressed in LPS-tolerant macrophages. Activation of Raf-1, located in the upstream portion of ERK cascades, was also suppressed by LPS-tolerance induction. These suppressions in LPS-tolerant macrophages were exhibited against stimulation by an LPS agonist like taxol, but not towards stimulation by an unrelated activator like phorbol ester (PMA). Activation of the transcription factor NF-κB, which is supposed to be one of the components of another important pathway for transduction of LPS-stimulated cytokine producing signals, was strongly suppressed and degradation of IκB, an inhibitor of NF-κB, was also severely diminished in LPS-tolerant macrophages. Although a monosaccharide lipid A analog, GLA-58, was able to stimulate macrophages to activate ERK proteins without cytokine production, pretreatment of macrophages with this compound suppressed both LPS-stimulated activation of ERK and cytokine production Furthermore, downregulation of LPS-uptake in LPS-tolerant macrophages was not observed Based on all these findings, LPS tolerance might be caused by the previous activation of some components on LPS-signaling pathways. This may then induce a refractory state in key LPS-signal transducer mols. located downstream of the cell membrane LPS receptor and upstream of the branching point in intracellular cascades for activation of MAPK and NF-κB, probably in some initial steps of intracellular signaling.

IT 137632-07-6, Erk1 kinase 137632-08-7, Erk2 kinase 155215-87-5, **Jnk** kinase 165245-96-5, p38 Map kinase

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(lipopolysaccharide tolerance in murine peritoneal macrophages induces downregulation of lipopolysaccharide signal transduction pathway through MAP kinase and NF-κB cascades)

L6 ANSWER 27 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:377983 CAPLUS
DN 131:183264
TI Activation of Mitogen-activated Protein Kinases in in vivo **Ischemia**/Reperfused Myocardium in Rats
AU Omura, Takashi; Yoshiyama, Minoru; Shimada, Takehiro; Shimizu, Naruhito; Kim, Shokei; Iwao, Hiroshi; Takeuchi, Kazuhide; Yoshikawa, Junichi
CS First Department of Internal Medicine, Osaka City University Medical School, Osaka, Japan
SO Journal of Molecular and Cellular Cardiology (**1999**), 31(6), 1269-1279
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic Press
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Activation of Mitogen-activated Protein Kinases in in vivo **Ischemia**/Reperfused Myocardium in Rats
SO Journal of Molecular and Cellular Cardiology (**1999**), 31(6), 1269-1279
CODEN: JMCDAY; ISSN: 0022-2828
AB In this study, we investigate the in vivo activation of mitogen-activated protein kinases (MAPK) as important signal transduction cascades observed after myocardial **ischemia**/reperfusion. Myocardial continuous **ischemia** and **ischemia**/reperfusion was produced in Wistar rats. The activities of MAPKs in the **ischemic** and **ischemia**/reperfused regions were measured using an in-gel kinase assay, an in vitro kinase assay and Western blot anal. Activator protein-1 (AP-1) DNA binding activity was determined using an electrophoretic mobility shift assay. DNA fragmentation was detected as DNA ladders by agarose gel electrophoresis. The p46JNK and p55JNK activities of continuous **ischemia** were significantly increased at 30 min (5.9 and 4.2 fold, resp.). Coronary reperfusion increased both p42ERK and p44ERK activities at 30 min (3.0 and 2.3 fold), and both p46JNK and p55JNK activities at 30 min (1.4 and 1.7 fold). The AP-1 DNA binding activities of continuous **ischemia** were significantly increased at 1, 3 and 7 days (28, 21 and 17 fold, resp.). Coronary reperfusion markedly decreased AP-1 DNA binding activities at 1 (41%) and 3 days (48%). Myocardial DNA fragmentation was considerably more enhanced by reperfusion than continuous **ischemia**. In conclusion, our present work provides the first in vivo evidence that ERK and **JNK** are activated by reperfusion from the activities of continuous **ischemia**. These signal transduction mechanisms may be partially responsible for the myocardial injury. (c) 1999 Academic Press.
ST MAP kinase heart **ischemia** reperfusion
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(AP-1 (activator protein 1); AP-1 DNA binding activity decrease and activation of mitogen-activated protein kinases and their signaling pathway in in vivo **ischemia**/reperfused myocardium in Rats)
IT Signal transduction, biological
(activation of mitogen-activated protein kinases in in vivo **ischemia**/reperfused myocardium in Rats)

IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fragmentation; activation of mitogen-activated protein kinases and their signaling pathway in in vivo **ischemia**/reperfused myocardium in Rats)
IT Reperfusion
(injury; activation of mitogen-activated protein kinases in in vivo **ischemia**/reperfused myocardium in Rats)
IT Heart, disease
(**ischemia**; activation of mitogen-activated protein kinases in in vivo **ischemia**/reperfused myocardium in Rats)
IT 165245-96-5, p38 MAP kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of mitogen-activated protein kinases and their signaling pathway in in vivo **ischemia**/reperfused myocardium in Rats)
IT 137632-07-6, p44 Mitogen-activated protein kinase 137632-08-7, p42 Mitogen-activated protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of mitogen-activated protein kinases in in vivo **ischemia**/reperfused myocardium in Rats)
IT 137632-07-6 137632-08-7
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of mitogen-activated protein kinases in in vivo **ischemia**/reperfused myocardium in Rats)
IT 155215-87-5, **JNK**-46 protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p46 and p55; activation of mitogen-activated protein kinases and their signaling pathway in in vivo **ischemia**/reperfused myocardium in Rats)

L6 ANSWER 28 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:339283 CAPLUS
DN 131:156612
TI c-Jun and the c-Jun amino-terminal kinases: bipotential components of the neuronal stress response
AU Herdegen, Thomas; Mielke, Kirsten; Kallunki, Tuula
CS Department of Pharmacology, University of Kiel, Kiel, Germany
SO Neuroscientist (**1999**), 5(3), 147-154
CODEN: NROSFJ; ISSN: 1073-8584
PB Lippincott Williams & Wilkins
DT Journal; General Review
LA English
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Neuroscientist (**1999**), 5(3), 147-154
CODEN: NROSFJ; ISSN: 1073-8584
AB A review with 68 refs. Expression of the inducible transcription factor c-Jun in neurons is a common finding after neuronal injury or "stress", such as **ischemia**, excitotoxicity, axon transection, UV irradiation, stimulation by cytokines, or production of such lipid messengers as ceramide. The neuronal "stress response" displays striking similarities to the stress response of other cell types and is characterized by the activation of programs that lead to apoptosis or survival. It is accepted knowledge that c-Jun can act as neuronal "killer" under in vitro conditions, but

there is also growing evidence that c-Jun is linked to neuronal repair or survival. The control of this dichotomous function of c-Jun is not fully understood. Similar to the expression of c-Jun, the transcriptional activation of c-Jun by N-terminal phosphorylation and the activation of the catalyzing c-Jun N-terminal kinases (**JNK**), also called stress activated protein kinases, can also be linked to both neuronal survival and apoptosis. The authors suggest a model for the control of gene transcription after neuronal stress with activation of **JNK** and phosphorylation of c-Jun as transcriptional prerequisites, and with associated partners as transcriptional effectors, e.g., by the expression and/or suppression of other transcription factors as ATF-2, c-Fos, or JunD. This scenario is complicated by the observation that activity of **JNK** does not lead automatically to c-Jun phosphorylation. The authors summarize here the role of c-Jun and **JNK** as down-stream mediators of neuronal stressors and place the function of these mols. in the context of other stressful stimuli and intraneuronal responses.

ST Jun transcription factor **JNK** kinase neuron stress response review

L6 ANSWER 29 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:292081 CAPLUS
Correction of: 1998:767023

DN 130:295044
Correction of: 130:166681

TI Sequential activation of activator protein-1-related transcription factors and **JNK** protein kinases may contribute to apoptotic death induced by transient hypoxia in developing brain neurons

AU Chihab, Rifki; Ferry, Celine; Koziel, Violette; Monin, Pierre; Daval, Jean-Luc

CS Universite Henri Poincare-Nancy 1, Nancy, Fr.

SO Molecular Brain Research (**1998**), 63(1), 105-120
CODEN: MBREE4; ISSN: 0169-328X

PB Elsevier Science B.V.

DT Journal

LA English

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Sequential activation of activator protein-1-related transcription factors and **JNK** protein kinases may contribute to apoptotic death induced by transient hypoxia in developing brain neurons

SO Molecular Brain Research (**1998**), 63(1), 105-120
CODEN: MBREE4; ISSN: 0169-328X

AB Previous studies have demonstrated that transient hypoxia (6 h) induces apoptotic death in cultured neurons isolated from the fetal rat forebrain. Since activation of c-Jun N-terminal kinases (JNKs) and subsequent phosphorylation of c-Jun are suspected to be involved in the apoptotic pathway in several cell types, the time course of activator protein-1 (AP-1) DNA-binding, in line with induction of the AP-1 components and **JNK** activation, was examined during hypoxia/reoxygenation in the same model. Gel shift anal. depicted the presence of functional AP-1 transcription factors in both control and hypoxic neurons. One hour after the onset of hypoxia, all AP-1 components were markedly overexpressed. They include c-Jun, Jun B, Jun D, c-Fos and Fos-related antigens. Whereas, only c-Jun remained elevated for up to 96 h post-reoxygenation, time at which neurons were injured, other gene products showed patterned induction/repression as hypoxia progressed and then during the post-reoxygenation period, with Fos-related antigens being finally induced at 96 h. Only JNK1 was constitutively detected in cultured neurons, and its expression was inhibited during hypoxia. Nonetheless, both JNK1 and JNK3 were markedly, but transiently, induced at 48 h post-reoxygenation, when apoptosis-related morphol. features became apparent. These data support the hypothesis that transient hypoxia, independently of

ischemia, may trigger apoptosis through **JNK** signaling pathway in developing brain neurons.

ST AP1 transcription factor **JNK** kinase apoptosis brain **ischemia**

L6 ANSWER 30 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:274818 CAPLUS
DN 131:57256
TI **Ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton
AU Baines, Christopher P.; Liu, Guang S.; Birincioglu, Mustafa; Critz, Stuart D.; Cohen, Michael V.; Downey, James M.
CS Departments of Physiology, Structural and Cellular Biology, and Medicine, University of South Alabama, Mobile, AL, 36688-0002, USA
SO American Journal of Physiology (**1999**), 276(4, Pt. 2), H1361-H1368
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI **Ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton
SO American Journal of Physiology (**1999**), 276(4, Pt. 2), H1361-H1368
CODEN: AJPHAP; ISSN: 0002-9513
AB Both mitochondrial ATP-sensitive K+ (KATP) channels and the actin cytoskeleton have been proposed to be end-effectors in **ischemic** preconditioning (PC). For evaluation of the participation of these proposed end effectors, rabbits underwent 30 min of regional **ischemia** and 3 h of reperfusion. PC by 5-min **ischemia** + 10-min reperfusion reduced infarct size by 60%. Diazoxide, a mitochondrial KATP-channel opener, administered before **ischemia** was protective. Protection was lost when diazoxide was given after onset of **ischemia**. Anisomycin, a p38/**JNK** activator, reduced infarct size, but protection from both diazoxide and anisomycin was abolished by 5-hydroxydecanoate (5-HD), an inhibitor of mitochondrial KATP channels. Isolated adult rabbit cardiomyocytes were subjected to simulated **ischemia** by centrifuging the cells into an oxygen-free pellet for 3 h. PC was induced by prior pelleting for 10 min followed by resuspension for 15 min. Osmotic fragility was assessed by adding cells to hypotonic (85 mosmol) Trypan blue. PC delayed the progressive increase in fragility seen in non-PC cells. Incubation with diazoxide or pinacidil was as protective as PC. Anisomycin reduced osmotic fragility, and this was reversed by 5-HD. Interestingly, protection by PC, diazoxide, and pinacidil could be abolished by disruption of the cytoskeleton by cytochalasin D. These data support a role for both mitochondrial KATP channels and cytoskeletal actin in protection by PC.
ST heart **ischemia** preconditioning actin mitochondria potassium channel
IT Potassium channel
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ATP-sensitive; **ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)
IT Biological transport
(channel-mediated; **ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)
IT Heart, disease
(**infarction**; **ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)

IT Heart, disease
(**ischemia**; **ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)
IT Mitochondria
Signal transduction, biological
(**ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)
IT Actins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)
IT Biological transport
(potassium; **ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)
IT 155215-87-5 165245-96-5, p38 MAP kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)
IT 7440-09-7, Potassium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)
IT 7440-09-7, Potassium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport; **ischemic** preconditioning depends on interaction between mitochondrial KATP channels and actin cytoskeleton)

L6 ANSWER 31 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:257512 CAPLUS
DN 131:43317
TI Aberrant CD3- and CD28-mediated signaling events in cord blood T cells are associated with dysfunctional regulation of Fas ligand-mediated cytotoxicity
AU Sato, Katsuaki; Nagayama, Hitomi; Takahashi, Tsuneo A.
CS Department of Cell Processing, Institute of Medical Science, University of Tokyo, Tokyo, 108-8639, Japan
SO Journal of Immunology (**1999**), 162(8), 4464-4471
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Immunology (**1999**), 162(8), 4464-4471
CODEN: JOIMA3; ISSN: 0022-1767
AB There have been numerous reports of decreased acute and chronic graft-vs.-host disease (GVHD) in patients receiving HLA-matched or HLA-disparate umbilical cord transplants. However, little is known about the mechanisms underlying the low incidence of GVHD in umbilical cord blood transplantation (CBT). In this study, the authors examined CD3- and CD28-mediated functional properties and signaling events in CB T cells (CBTCs). Dual stimulation of peripheral blood TCs (PBTCs) and bone marrow TCs (BMTCs) with mAbs to CD3- and CD28-induced expression of Fas ligand (FasL), as well as CD25 and CD154 (CD40L), whereas defective induction of these activation-associated cell surface mols. were observed in CBTCs. Engagement of both CD3 and CD28 induced FasL-mediated cytotoxicity in peripheral blood TCs (PBTCs) but not CBTCs; however, both of these tissue

sources possess intrinsically similar proliferative responsiveness. Anal. of CD3- and CD28-induced signal transduction revealed a deficiency in signaling events that involved repressed tyrosine phosphorylation and enzymic activities of a family of mitogen-activated protein kinases, extracellular signal-regulated kinase 2, stress-activated protein kinase/c-jun N-terminal kinase (SAPK/**JNK**), and p38mapk, as well as p56lck and ZAP-70 in CBTCs compared with those in PBTCs. These results suggest that CD3- and CD28-mediated signaling events blockage in CBTCs may be responsible for dysfunction of FasL-mediated cytotoxicity and lead to the low incidence of severe GVHD in CBT.

IT **Transplant** and Transplantation
Transplant and Transplantation
(allotransplant, bone marrow; TCR/CD3- and CD28-mediated signaling events in cord blood T-cells are associated with dysfunctional regulation of FasL-mediated effector function in relation to graft-vs. host reaction in)

IT **Transplant** and Transplantation
(graft-vs.-host reaction; TCR/CD3- and CD28-mediated signaling events in cord blood T-cells are associated with dysfunctional regulation of FasL-mediated effector function in relation to)

L6 ANSWER 32 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:249101 CAPLUS
DN 130:277326
TI Methods for the modulation of neovascularization and/or the growth of collateral arteries and/or other arteries from preexisting arteriolar connections using a colony stimulating factor (CSF) or a CSF inhibitor
IN Buschmann, Ivo R.; Schaper, Wolfgang
PA Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V., Germany
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9917798	A1	19990415	WO 1998-EP6233	19981001	<--
	W: CA, JP, US					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	CA 2304354	AA	19990415	CA 1998-2304354	19981001	<--
	EP 1019082	A1	20000719	EP 1998-951483	19981001	
	EP 1019082	B1	20040107			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2001518517	T2	20011016	JP 2000-514667	19981001	
	AT 257392	E	20040115	AT 1998-951483	19981001	
	US 2003147862	A1	20030807	US 2000-509764	20001016	
PRAI	EP 1997-117155	A	19971002			
	WO 1998-EP6233	W	19981001			

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI WO 9917798 A1 **19990415**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9917798	A1	19990415	WO 1998-EP6233	19981001	<--
	W: CA, JP, US					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	CA 2304354	AA	19990415	CA 1998-2304354	19981001	<--
	EP 1019082	A1	20000719	EP 1998-951483	19981001	
	EP 1019082	B1	20040107			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2001518517	T2	20011016	JP 2000-514667	19981001
AT 257392	E	20040115	AT 1998-951483	19981001
US 2003147862	A1	20030807	US 2000-509764	20001016

IT Heart, disease
(**infarction**; methods for modulation of neovascularization and/or growth of collateral arteries and/or other arteries in subjects suffering from a vascular disease, a cardiac infarct, or a stroke using a CSF)

IT 142805-58-1, MAPK kinase 155215-87-5, Protein kinase **JNK**
155215-87-5, Stress-activated protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(method for the treatment of tumors with an agent that suppresses neovascularization and/or the growth of collateral arteries and/or other arteries through inhibition of the biol. activity of a CSF or signaling by CSF)

L6 ANSWER 33 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:244741 CAPLUS
DN 130:265957
TI JNK3 function in excitotoxicity and its use in treating related disorders and screening for modulators
IN Davis, Roger J.; Flavell, Richard A.; Rakic, Pasko; Whitmarsh, Alan J.; Kuan, Chia-Yin; Yang, Di
PA University of Massachusetts, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9918193	A1	19990415	WO 1998-US20904	19981005	<--
W: AU, CA, JP, KR					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 2003023990	A1	20030130	US 1998-165522	19981002	
CA 2302874	AA	19990415	CA 1998-2302874	19981005	<--
AU 9911860	A1	19990427	AU 1999-11860	19981005	<--
AU 756401	B2	20030109			
EP 1027429	A1	20000816	EP 1998-954937	19981005	
R: DE, GB					
JP 2001519146	T2	20011023	JP 2000-514991	19981005	
PRAI US 1997-60995P	P	19971003			
WO 1998-US20904	W	19981005			

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI WO 9918193 A1 **19990415**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9918193	A1	19990415	WO 1998-US20904	19981005	<--
W: AU, CA, JP, KR					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 2003023990	A1	20030130	US 1998-165522	19981002	
CA 2302874	AA	19990415	CA 1998-2302874	19981005	<--
AU 9911860	A1	19990427	AU 1999-11860	19981005	<--
AU 756401	B2	20030109			
EP 1027429	A1	20000816	EP 1998-954937	19981005	

R: DE, GB
JP 2001519146 T2 20011023 JP 2000-514991 19981005
AB The c-Jun N-terminal kinase (**JNK**) group of MAP kinases are activated by exposure of cells to environmental stress. The role of **JNK** in the brain was examined by targeted disruption of the gene that encodes the neuronal isoform JNK3. JNK3 plays a role in stress-induced seizure activity, AP-1 transcriptional activation, and kainate-induced apoptosis of hippocampal neurons. Mice lacking the JNK3 gene develop normally and are resistant to excitotoxic damage. Thus, JNK3 is a mediator of kainate-glutamate excitotoxicity and a target for limiting or preventing excitotoxic damage. Methods of screening for mols. and compds. that decrease JNK3 expression or activity are described. Such mols. or compds. are useful for treating disorders involving excitotoxicity such as seizure disorders, Alzheimer's disease, Huntington disease, Parkinson's disease, and **ischemia**.
IT Anti-Alzheimer's agents
Anti-**ischemic** agents
Anticonvulsants
Antiparkinsonian agents
(screening for; JNK3 function in excitotoxicity and its use in treating related disorders and screening for modulators)

L6 ANSWER 34 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:233811 CAPLUS
DN 130:276748
TI Methods and compositions using mitogen protein phosphatase inhibitors for treating, preventing and/or delaying **ischemic** cell death
IN Schaper, Wolfgang; Htun, Patrik; Barancik, Miroslav
PA Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V., Germany
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9916457	A2	19990408	WO 1998-EP6269	19981001 <--
WO 9916457	A3	19990722		

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI WO 1998-EP6269 19981001
TI Methods and compositions using mitogen protein phosphatase inhibitors for treating, preventing and/or delaying **ischemic** cell death
PI WO 9916457 A2 **19990408**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9916457	A2	19990408	WO 1998-EP6269	19981001 <--
WO 9916457	A3	19990722		

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AB Described is the modulation of **ischemic** cell death. In particular, pharmaceutical compns. are provided comprising an inhibitor of mitogen protein phosphatases (MKP), and/or a nucleic acid mol. encoding the inhibitor, which are particularly useful for treating, preventing and/or delaying **ischemic** cell death. Furthermore, methods for treating, preventing and/or delaying **ischemic** cell death comprising contacting organs, tissue or cells with an inhibitor of mitogen protein phosphatases (MKP), and/or a nucleic acid mol. encoding the inhibitor, are described.
ST mitogen protein phosphatase inhibitor **ischemic** cell death

IT Drugs
Radiotherapy
Surgery
(artery-damaging; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Cytoprotective agents
(cardioprotective; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Arteriosclerosis
Blood vessel, disease
(cell death from; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Brain, disease
(cerebrovascular, cerebral occlusive disease; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Artery, disease
(coronary; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Artery, disease
(damage; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Heart, disease
(**infarction**, cell death from; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Drug delivery systems
(injections, i.m.; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Drug delivery systems
(injections, i.v.; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Drug delivery systems
(injections, s.c.; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Drug delivery systems
(intracoronary and others; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT **Ischemia**
(**ischemic** preconditioning and tolerance; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Mesentery
(mesenterial artery insufficiency; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Nucleic acids
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mitogen protein phosphatase inhibitor-encoding; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)
IT Animal tissue
Anti-**ischemic** agents
Cell death
Cytoprotective agents
Dephosphorylation, biological
Gene therapy
Organ, animal
Peptidomimetics
Phosphorylation, biological
Signal transduction, biological

(mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT Antibodies
Growth factors, animal
Hormones, animal, biological studies
Ligands
Organic compounds, biological studies
Peptide nucleic acids
Peptides, biological studies
Proteins, general, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT Kidney, disease
(obstruction, renal occlusive disease; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT Blood vessel, disease
(occlusion, peripheral and visceral occlusive disease; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT Eye, disease
(ophthalmic or retinal occlusion; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT Drug delivery systems
(solns., i.p.; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT Brain, disease
(stroke, cell death from; mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT 9025-75-6, Protein serine-threonine phosphatase 137632-07-6, ERK1 protein kinase 137632-07-6 137632-08-7, ERK2 protein kinase 137632-08-7 155215-87-5, **JNK** kinase 165245-96-5, p38 MAP kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT 78111-17-8, Okadaic acid 78111-17-8D, Okadaic acid, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

IT 150605-50-8, Mitogen activated protein kinase phosphatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mitogen protein phosphatase inhibitors for treatment and prevention of **ischemic** cell death)

L6 ANSWER 35 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:227336 CAPLUS
DN 131:14336
TI Regulation of extracellular-signal regulated kinase and c-jun N-terminal kinase by G-protein-linked muscarinic acetylcholine receptors
AU Wylie, Paul G.; Challiss, R. A. John; Blank, Jonathan L.
CS Department of Cell Physiology and Pharmacology, University of Leicester School of Medicine, Leicester, LE1 9HN, UK

SO Biochemical Journal (**1999**), 338(3), 619-628
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Biochemical Journal (**1999**), 338(3), 619-628
CODEN: BIJOAK; ISSN: 0264-6021
AB Extracellular signal-regulated kinases (ERKs) and c-Jun N-terminal kinases (JNKs, or stress-activated protein kinases) are activated by diverse extracellular signals and mediate a variety of cellular responses, including mitogenesis, differentiation, **hypertrophy**, inflammatory reactions and apoptosis. We have examined the involvement of Ca2+ and protein kinase C (PKC) in ERK and **JNK** activation by the human G-protein-coupled m2 and m3 muscarinic acetylcholine receptors (mAChR) expressed in Chinese hamster ovary (CHO) cells. We show that the Ca2+-mobilizing m3 AChR is efficiently coupled to **JNK** and ERK activation, whereas the m2 AChR activates ERK but not **JNK**. Activation of **JNK** in CHO-m3 cells by the agonist methacholine (MCh) was delayed in onset and more sustained relative to that of ERK in either CHO-m2 or CHO-m3 cells. The EC50 values for MCh-induced ERK activation in both cell types were essentially identical and similar to that for **JNK** activation in CHO-m3 cells, suggesting little amplification of the response. Agonist-stimulated Ins(1,4,5)P3 accumulation in CHO-m3 cells was insensitive to pertussis toxin (PTX), consistent with a Gq/phosphoinositide-specific phospholipase C-β mediated pathway, whereas a significant component of ERK and **JNK** activation in CHO-m3 cells was PTX-sensitive, indicating Gi/o involvement. Using manipulations that prevent receptor-mediated extracellular Ca2+ influx and intracellular Ca2+-store release, we also show that ERK activation by m2 and m3 receptors is Ca2+-independent. In contrast, a significant component (>50%) of **JNK** activation mediated by the m3 AChR was dependent on Ca2+, mainly derived from extracellular influx. PKC inhibition and down-regulation studies suggested that **JNK** activation was neg. regulated by PKC. Conversely, ERK activation by both m2 and m3 AChRs required PKC, suggesting a novel mechanism for PKC activation by PTX-sensitive m2 AChRs. In summary, mAChRs activate **JNK** and ERK via divergent mechanisms involving either Ca2+ or PKC resp.

L6 ANSWER 36 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:226793 CAPLUS
DN 131:72326
TI Protein kinase cascades in intracellular signaling by interleukin-1 and tumor necrosis factor
AU Saklatvala, Jeremy; Dean, Jon; Finch, Andrew
CS Division of Cell Signalling, Kennedy Institute of Rheumatology, London, W6 8LH, UK
SO Biochemical Society Symposia (**1999**), 64(Cellular Responses to Stress), 63-77
CODEN: BSSYAT; ISSN: 0067-8694
PB Portland Press Ltd.
DT Journal; General Review
LA English
RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Biochemical Society Symposia (**1999**), 64(Cellular Responses to Stress), 63-77
CODEN: BSSYAT; ISSN: 0067-8694
AB A review with 65 refs. Interleukin 1 (IL-1) and tumor necrosis factor (TNF) are major mediators of inflammation, with similar actions. Their

receptor mechanisms and downstream pathways are reviewed. They activate several protein kinases in fibroblasts, including the three types of mitogen-activated protein kinase (MAPK), the kinase of the inhibitor of nuclear factor-κB (IκBK), and the TNF-/IL-1-activated β-casein kinase. Cultured cells show a broader spectrum of kinase activation by IL-1 than tissues in vivo, suggesting that the receptors connect to more pathways in proliferating cells than in resting differentiated cells. The c-Jun N-terminal kinase (**JNK**) is strongly activated by IL-1 in tissues. In rabbit liver this is mediated by MAPK kinase 7; the upstream kinase is unidentified. Little is known of downstream MAPK targets in inflammation. Inhibitor expts. suggest that p38MAPK mediates induction of cyclo-oxygenase-2 and metalloproteinases by IL-1, and of TNF, IL-1 and cyclo-oxygenase-2 by **endotoxin** (in monocytes). P38MAPK is needed for induction of the mRNAs (except IL-1 mRNA).

IT 142243-02-5, Map kinase 142805-58-1, Mapk kinase 155215-87-5, **Jnk** kinase 159606-08-3, iκb Kinase 165245-96-5, p38 Map kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protein kinase cascades in intracellular signaling by interleukin-1 and tumor necrosis factor)

L6 ANSWER 37 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:214970 CAPLUS
DN 131:17368
TI Aberrant neurofilament phosphorylation in sensory neurons of rats with diabetic neuropathy
AU Fernyhough, Paul; Gallagher, Alex; Averill, Sharon A.; Priestley, John V.; Hounsom, Luke; Patel, Jyoti; Tomlinson, David R.
CS Division of Neuroscience, School of Biological Sciences, University of Manchester, Manchester, M13 9PT, UK
SO Diabetes (**1999**), 48(4), 881-889
CODEN: DIAEAZ; ISSN: 0012-1797
PB American Diabetes Association
DT Journal
LA English
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Diabetes (**1999**), 48(4), 881-889
CODEN: DIAEAZ; ISSN: 0012-1797
AB Aberrant neurofilament phosphorylation occurs in many neurodegenerative diseases, and in this study, two animal models of type 1 **diabetes** -the spontaneously diabetic BB rat and the streptozocin-induced diabetic rat-have been used to determine whether such a phenomenon is involved in the etiol. of the sym. sensory polyneuropathy commonly associated with **diabetes**. There was a two- to threefold elevation of neurofilament phosphorylation in lumbar dorsal root ganglia (DRG) of diabetic rats that was localized to perikarya of medium to large neurons using immunocytochem. Addnl., **diabetes** enhanced neurofilament M phosphorylation by 2.5-fold in sural nerve of BB rats. Neurofilaments are substrates of the mitogen-activated protein kinase (MAPK) family, which includes c-jun NH2-terminal kinase (**JNK**) or stress-activated protein kinase (SAPK1) and extracellular signal-regulated kinases (ERKs) 1 and 2. **Diabetes** induced a significant three- to fourfold increase in phosphorylation of a 54-kDa isoform of **JNK** in DRG and sural nerve, and this correlated with elevated c-Jun and neurofilament phosphorylation. In **diabetes**, ERK phosphorylation was also increased in the DRG, but not in sural nerve. Immunocytochem. showed that **JNK** was present in sensory neuron perikarya and axons. Motoneuron perikarya and peroneal nerve of diabetic rats showed no evidence of

increased neurofilament phosphorylation and failed to exhibit phosphorylation of **JNK**. It is hypothesized that in sensory neurons of diabetic rats, aberrant phosphorylation of neurofilament may contribute to the distal sensory axonopathy observed in **diabetes**.

ST **diabetes** neuropathy neurofilament protein phosphorylation

IT **Diabetes** mellitus
(insulin-dependent; aberrant neurofilament phosphorylation in sensory neurons of rats with diabetic neuropathy)

L6 ANSWER 38 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:214701 CAPLUS
DN 131:16731
TI Molecular cloning of multiple splicing variants of JIP-1 preferentially expressed in brain
AU Kim, In-Jung; Lee, Ko-Woon; Park, Byung Young; Lee, Ja-Kyeong; Park, Jihyun; Choi, In Young; Eom, Soo-Jung; Chang, Tong-Shin; Kim, Myung Jin; Yeom, Young Il; Chang, Sung Key; Lee, Young-Don; Choi, Eui-Ju; Han, Pyung-Lim
CS Laboratory for Basic Research, Hanhyo Institutes of Technology, Taejon, S. Korea
SO Journal of Neurochemistry (**1999**), 72(4), 1335-1343
CODEN: JONRA9; ISSN: 0022-3042
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Neurochemistry (**1999**), 72(4), 1335-1343
CODEN: JONRA9; ISSN: 0022-3042
AB Stress-activated protein kinase/c-Jun N-terminal kinase (SAPK/**JNK**) is activated by a variety of cellular or environmental stresses. Proper regulation of the SAPK/**JNK** pathway may be critical for cell survival or death under various conditions. In this study, the authors report the mol. cloning of novel isoforms of JIP-1, which harbor a putative phosphotyrosine interaction domain and a helix-loop-helix domain, as well as an SH3 homologous region in the C terminus. Northern anal. indicates that transcription variant jip-1 is expressed in brain and kidney and transcription variants jip-2 and jip-3 are specifically expressed in brain. In situ hybridization data showed that the hybridized jip messages were heavily concentrated in adult brain, and were particularly enriched in the cerebral cortex and hippocampus, the brain regions vulnerable to pathol. states such as hypoxia-**ischemia**, epilepsy, and Alzheimer's disease. All the deduced protein products of the jip transcription variants appear to have a similar property in that they inhibit the SAPK/**JNK** stimulation when overexpressed. Inhibition of SAPK activation by overexpression of the novel isoform JIP-2a resulted in suppression of etoposide-induced cell death in a neuroglioma cell line, N18TG. These findings suggest that JIP may play an important role in regulation of the SAPK pathway that is involved in stress-induced cellular responses.

ST **JNK** interacting protein JIP1 isoforms brain; cDNA sequence JIP protein isoforms; rat cDNA sequence JIP protein isoforms; mouse cDNA sequence JIP protein isoforms; SAPK kinase interacting protein SKIP isoforms

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(JIP-1b (**JNK**-interacting protein 1b); mol. cloning of splice variants of c-Jun N-terminal kinase-regulating protein JIP-1 and preferential expression in brain)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP

(Properties); BIOL (Biological study); OCCU (Occurrence)
(JIP-1c (**JNK**-interacting protein 1c); mol. cloning of splice variants of c-Jun N-terminal kinase-regulating protein JIP-1 and preferential expression in brain)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(JIP-2a (**JNK**-interacting protein 2a); mol. cloning of splice variants of c-Jun N-terminal kinase-regulating protein JIP-1 and preferential expression in brain)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(JIP-2b (**JNK**-interacting protein 2b); mol. cloning of splice variants of c-Jun N-terminal kinase-regulating protein JIP-1 and preferential expression in brain)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(JIP-3 (**JNK**-interacting protein 3); mol. cloning of splice variants of c-Jun N-terminal kinase-regulating protein JIP-1 and preferential expression in brain)

IT 146838-31-5, SAPK kinase 155215-87-5, **JNK** kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interaction with JIP isoforms; mol. cloning of splice variants of c-Jun N-terminal kinase-regulating protein JIP-1 and preferential expression in brain)

L6 ANSWER 39 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:194265 CAPLUS
DN 130:233822
TI Rin2, a novel inhibitor of Ras-mediated signaling and a cDNA encoding it
IN Tam, See-ying; Tsai, Mindy; Galli, Stephen J.
PA Beth Israel Deaconess Medical Center, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9913079	A1	19990318	WO 1998-US19056	19980911 <--
	W: AU, CA, JP, US, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5965707	A	19991012	US 1997-942819	19971002 <--
	AU 9893156	A1	19990329	AU 1998-93156	19980911 <--
	US 6500942	B1	20021231	US 2000-522955	20000310
PRAI	US 1997-58520P	P	19970911		
	US 1997-942819	A2	19971002		
	WO 1998-US19056	W	19980911		

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI WO 9913079 A1 **19990318**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9913079	A1	19990318	WO 1998-US19056	19980911 <--
	W: AU, CA, JP, US, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5965707	A	19991012	US 1997-942819	19971002 <--

AU 9893156 A1 19990329 AU 1998-93156 19980911 <--
US 6500942 B1 20021231 US 2000-522955 20000310

IT Autoimmune disease
Dermatomyositis
Multiple sclerosis
Psoriasis
Rheumatoid arthritis
Sarcoidosis
Sjogren's syndrome
Transplant rejection
(Rin-2 effectors as immunosuppressants for treatment of; Rin2, novel inhibitor of Rás-mediated signaling and cDNA encoding it)

IT **Transplant** and Transplantation
(graft-vs.-host reaction, Rin-2 effectors as immunosuppressants for treatment of; Rin2, novel inhibitor of Ras-mediated signaling and cDNA encoding it)

IT **Diabetes** mellitus
(insulin-dependent, Rin-2 effectors as immunosuppressants for treatment of; Rin2, novel inhibitor of Ras-mediated signaling and cDNA encoding it)

IT 155215-87-5, **JNK** kinase 165245-96-5, p38 MAP kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(activation of, as indicator in screening for effectors of Rin-2; Rin2, novel inhibitor of Ras-mediated signaling and cDNA encoding it)

L6 ANSWER 40 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:185685 CAPLUS
DN 131:16907
TI **JNK** activation and apoptosis during **ischemia**
-reperfusion
AU Onishi, I.; Shimizu, K.; Tani, T.; Hashimoto, T.; Miwa, K.
CS Department of Surgery, Kanazawa University, Kanazawa, 930-0974, Japan
SO Transplantation Proceedings (**1999**), 31(1/2), 1077-1079
CODEN: TRPPA8; ISSN: 0041-1345
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI **JNK** activation and apoptosis during **ischemia**
-reperfusion
SO Transplantation Proceedings (**1999**), 31(1/2), 1077-1079
CODEN: TRPPA8; ISSN: 0041-1345
AB The relationship between **JNK** activity and apoptosis c-Jun N-terminal kinase (**JNK**) during **ischemia**-reperfusion of mouse liver was studied. The effect of antioxidants was also examined **JNK** was translocated and phosphorylated during **ischemia** -reperfusion in mouse liver. **JNK** activation and expression of apoptotic cells during **ischemia**-reperfusion were suppressed by premedication with D-α-tocopherol. Thus, oxidative stress could mediate the signaling pathway leading to **JNK** activation and apoptosis.
ST **JNK** apoptosis oxidative stress liver **ischemia** reperfusion
IT Apoptosis
Ischemia
(**JNK** activation and apoptosis during **ischemia** -reperfusion)
IT Reperfusion
(injury; **JNK** activation and apoptosis during **ischemia**

-reperfusion)
IT Oxidative stress, biological
(role of oxidative stress in signaling pathway leading to **JNK** activation and apoptosis)
IT 155215-87-5, **JNK** kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**JNK** activation and apoptosis during **ischemia** -reperfusion)
IT 59-02-9, D-α-Tocopherol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(role of oxidative stress in signaling pathway leading to **JNK** activation and apoptosis)

L6 ANSWER 41 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:158551 CAPLUS
DN 130:310053
TI Stretch-induced overproduction of fibronectin in mesangial cells is mediated by the activation of mitogen-activated protein kinase
AU Ishida, Takeshi; Haneda, Masakazu; Maeda, Shiro; Koya, Daisuke; Kikkawa, Ryuichi
CS Third Department of Medicine, Shiga University of Medical Science, Otsu, 520-2192, Japan
SO Diabetes (**1999**), 48(3), 595-602
CODEN: DIAEAZ; ISSN: 0012-1797
PB American Diabetes Association
DT Journal
LA English
RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Diabetes (**1999**), 48(3), 595-602
CODEN: DIAEAZ; ISSN: 0012-1797
AB An excessive production of extracellular matrix (ECM) proteins in glomerular mesangial cells is considered to be responsible for the development of mesangial expansion seen in diabetic nephropathy. Mech. stretch due to glomerular hypertension has been proposed as one of the factors leading to an increase in the production of ECM proteins in mesangial cells, but the precise mechanism of stretch-induced overprodn. of ECM proteins has not been elucidated. Herein, we provide the evidence that mitogen-activated protein kinase (MAPK) may play a key role in the overprodn. of fibronectin (FN) in mesangial cells exposed to mech. stretch. MAPK, also termed extracellular signal-regulated kinase (ERK) and c-Jun NH2-terminal kinase (**JNK**), was activated by mech. stretch in time- and intensity-dependent manners. Stretch-induced activation of ERK was inhibited by herbimycin A, a tyrosine kinase inhibitor, but not by GF109203X or calphostin C, the inhibitors of protein kinase C. Mech. stretch also enhanced DNA-binding activity of AP-1, and this enhancement was inhibited by PD98059, an inhibitor of MAPK or ERK kinase (MEK). Furthermore, mech. stretch stimulated the expression of FN mRNA followed by a significant increase in its protein accumulation. PD98059 could prevent stretch-induced increase in the expression of FN mRNA and protein. These results indicate that the activation of ERK may mediate the overprodn. of ECM proteins in mesangial cells exposed to mech. stretch, an in vitro model for glomerular hypertension seen in **diabetes**.
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1); mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model

for glomerular hypertension seen in **diabetes**)

IT Kidney, disease
(diabetic nephropathy; mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model for glomerular hypertension seen in **diabetes**)

IT Kidney
(mesangium; mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model for glomerular hypertension seen in **diabetes**)

IT Disease models
(mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model for glomerular hypertension seen in **diabetes**)

IT Fibronectins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model for glomerular hypertension seen in **diabetes**)

IT mRNA
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model for glomerular hypertension seen in **diabetes**)

IT Strain
(stretch; mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model for glomerular hypertension seen in **diabetes**)

IT 142243-02-5, Mitogen-activated protein kinase 155215-87-5
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model for glomerular hypertension seen in **diabetes**)

IT 80449-02-1, Tyrosine kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mitogen-activated protein kinase role in stretch-induced overprodn. of fibronectin in mesangial cells as model for glomerular hypertension seen in **diabetes**)

L6 ANSWER 42 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:141367 CAPLUS
DN 131:42383
TI Lysophosphatidylcholine activates mitogen-activated protein kinases by a tyrosine kinase-dependent pathway in bovine aortic endothelial cells
AU Ozaki, Harunobu; Ishii, Kenji; Arai, Hidenori; Kume, Noriaki; Kita, Toru
CS Graduate School of Medicine, Department of Geriatric Medicine, Kyoto University, Sakyo-ku, Shogoin, Kyoto, 606-8397, Japan
SO Atherosclerosis (Shannon, Ireland) (**1999**), 143(2), 261-266
CODEN: ATHSBL; ISSN: 0021-9150
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Atherosclerosis (Shannon, Ireland) (**1999**), 143(2), 261-266
CODEN: ATHSBL; ISSN: 0021-9150
AB Lysophosphatidylcholine (lyso-PC) is a major component of an atherogenic

lipoprotein. In this study, to investigate the involvement of mitogen-activated protein kinases in the signaling pathway by lyso-PC in endothelial cells, we measured the activity of extracellular signal-regulated kinase (ERK) and c-Jun N-terminal kinase (**JNK**) in bovine aortic endothelial cells. Lyso-PC activated ERK and **JNK** in a dose-dependent manner. However, the time courses of activation of these kinases were different. ERK and **JNK** activation by lyso-PC was inhibited by a tyrosine kinase inhibitor, herbimycin A, but not by a protein kinase C (PKC) specific inhibitor. We conclude, therefore, that lyso-PC-mediated ERK and **JNK** activation is caused by a tyrosine kinase-dependent mechanism, but not conventional types of PKC-dependent mechanisms.

ST lysophosphatidylcholine ERK **JNK** tyrosine kinase vascular endothelium **atherosclerosis**

IT **Atherosclerosis**
Cattle
Signal transduction, biological
(lysophosphatidylcholine activates mitogen-activated protein kinases by a tyrosine kinase-dependent pathway in bovine aortic endothelial cells)

L6 ANSWER 43 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:127504 CAPLUS
DN 130:310109
TI Delayed neuronal cell death in the rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway
AU Ozawa, Hiroshi; Shioda, Seiji; Dohi, Kenji; Matsumoto, Hiroaki; Mizushima, Hidekatsu; Ji Zhou, Cheng; Funahashi, Hisayuki; Nakai, Yasumitsu; Nakajo, Shigeo; Matsumoto, Kiyoshi
CS Department of Neurosurgery, Showa University School of Medicine, Tokyo, Japan
SO Neuroscience Letters (**1999**), 262(1), 57-60
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Neuroscience Letters (**1999**), 262(1), 57-60
CODEN: NELED5; ISSN: 0304-3940
AB Transient global **ischemia** caused by 5 min of cardiac arrest induced delayed neuronal cell death (apoptosis) in the CA1 region of the rat hippocampus. To characterize the mol. mechanisms that regulate apoptosis in vivo, the contributions to cell death of mitogen-activated protein kinase family members were examined in the hippocampal region after brain **ischemia**-reperfusion. **Ischemia**-reperfusion led to a strong activation of the **JNK**/SAPK (c-Jun NH2-terminal protein kinase/stress activated protein kinase), ERK (extracellular signal-regulated kinase), and p38 enzymes. These results with other previous studies suggest that the activation of **JNK**/SAPK in accordance with p38 contributes to the induction of apoptosis in CA1 neurons.

ST neuron death hippocampus **ischemia** MAP kinase signal transduction

IT Nerve, disease
(death; delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

IT Apoptosis
Signal transduction, biological
(delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

IT Brain, disease

(hippocampus, **ischemia**; delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

IT Brain
(hippocampus, sector CA1; delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

IT Brain, disease
(**ischemia**; delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

IT Cell death
(neuron; delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p38; delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

IT Nerve
(pyramidal cell; delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

IT 142243-02-5, Mitogen-activated protein kinase 155215-87-5
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(delayed neuronal cell death in **ischemic** rat hippocampus is mediated by the mitogen-activated protein kinase signal transduction pathway)

L6 ANSWER 44 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:125336 CAPLUS
DN 130:321164
TI Angiotensin II signaling in vascular smooth muscle cells under high glucose conditions
AU Natarajan, Rama; Scott, Stephen; Bai, Wei; Yerneni, Kiran Kumar V.; Nadler, Jerry
CS Gonda Diabetes Center, City of Hope Medical Center, Duarte, CA, USA
SO Hypertension (**1999**), 33(1, Pt. 2), 378-384
CODEN: HPRTDN; ISSN: 0194-911X
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Hypertension (**1999**), 33(1, Pt. 2), 378-384
CODEN: HPRTDN; ISSN: 0194-911X
AB The mechanisms responsible for the accelerated cardiovascular disease in **diabetes**, as well as the increased hypertrophic effects of angiotensin II (Ang II) under hyperglycemic conditions, are not very clear. The authors examined whether the culture of vascular smooth muscle cells (VSMC) under hyperglycemic conditions to simulate the diabetic state can lead to increased activation of key growth- and stress-related kinases, such as the mitogen-activated protein kinases (MAPKs), in the basal state and in response to Ang II. Treatment of porcine VSMC for short time periods (0.5 to 3 h) with high glucose (HG; 25 mmol/L) markedly increased the activation of the extracellular signal-regulated kinase (ERK1/2) and c-Jun/N-terminal kinase (**JNK**) relative to cells

cultured in normal glucose (NG; 5.5 mmol/L). The p38 MAPK also was activated by HG, and this effect remained sustained for several hours. Ang II treatment increased the activity of all 3 families of MAPKs. Ang II-induced ERK activation was potentiated nearly 2-fold in cells treated with HG for 0.5 h. However, Ang II-induced **JNK** was not altered. In VSMC cultured for 24 h with HG, Ang II and HG displayed an additive response on p38 MAPK activity. MAPKs can lead to activation of transcription factors such as activator protein-1 (AP-1). HG alone significantly increased AP-1 DNA-binding activity. Furthermore, Ang II and HG combined had additive effects on AP-1 activity. These results suggest that increased activation of specific MAPKs and downstream transcription factors, such as AP-1, may be key mechanisms for the increased VSMC growth potential of HG alone and of Ang II under HG conditions.

IT **Diabetes** mellitus
Hyperglycemia
(angiotensin II signaling in vascular smooth muscle cells under high glucose conditions in relation to hyperglycemia and **diabetes**)

L6 ANSWER 45 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:125321 CAPLUS
DN 130:336722
TI Interleukin-1β regulation of the human brain natriuretic peptide promoter involves Ras-, Rac-, and p38 kinase-dependent pathways in cardiac myocytes
AU He, Quan; LaPointe, Margot C.
CS Hypertension and Vascular Research Division, Henry Ford Hospital, Detroit, MI, 48202-2689, USA
SO Hypertension (**1999**), 33(1, Pt. 2), 283-289
CODEN: HPRTDN; ISSN: 0194-911X
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Hypertension (**1999**), 33(1, Pt. 2), 283-289
CODEN: HPRTDN; ISSN: 0194-911X
AB Because both the brain natriuretic peptide (BNP) gene and the cytokine interleukin-1β (IL-1β) are induced in the infarcted myocardium, localized production of IL-1β may regulate the BNP gene. The authors tested whether (1) IL-1β regulates the human BNP promoter, (2) cis elements in the proximal promoter respond to IL-1β, and (3) mitogen-activated protein kinase (MAPK) signaling pathways [p42/44, c-jun (**JNK**) and p38 kinase] are involved. The authors transferred the hBNP promoter coupled to a luciferase reporter gene or constructs with mutations in the proximal promoter GATA and M-CAT elements into neonatal rat ventricular myocytes and treated the cells with IL-1β for 24 h. IL-1β-stimulated hBNP luciferase activity was eliminated by pretreatment with the transcription inhibitor actinomycin D. Both the p38 kinase inhibitor SB205380 (SB) and cotransfection of a dominant-neg. mutant of p38 kinase reduced IL-1β stimulation of the hBNP promoter. Dominant-neg. mutants of Ras and Rac inhibited IL-1β-stimulated hBNP luciferase activity by 64% and 90%, resp. Constitutively active forms of Rac and MKK6, the immediate upstream activator of p38, were stimulatory; however, only the effect of MKK6 was inhibited by SB. Neither the p42/44 nor the **JNK** pathway was involved in the action of IL-1β. Both IL-1β and MKK6 activation of the hBNP promoter were partially reduced when the promoter contained a mutated M-CAT element. Thus, (1) IL-1β is a transcriptional activator of the hBNP promoter; (2) IL-1β acts through a Ras-dependent pathway not coupled to activation of p42/44 MAPK or **JNK**; (3) IL-1β acts via a Rac-dependent pathway, but the downstream effector is not known; and (4) IL-1β

activation of p38 kinase is partially involved in regulation of the hBNP promoter, targeting the proximal M-CAT element.

IT Heart, disease
(**infarction**; interleukin-1β regulation of human brain natriuretic peptide promoter involves Ras-, Rac-, and p38 kinase-dependent pathways in cardiac myocytes)

L6 ANSWER 46 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:69151 CAPLUS
DN 130:262380
TI PACAP protects hippocampal neurons against apoptosis: involvement of **JNK**/SAPK signaling pathway
AU Shioda, Seiji; Ozawa, Hiroshi; Dohi, Kenji; Mizushima, Hidekatsu; Matsumoto, Kiyoshi; Nakajo, Shigeo; Takaki, Atsushi; Zhou, Cheng Ji; Nakai, Yasumitsu; Arimura, Akira
CS Department of Anatomy, Showa University School of Medicine, Tokyo, 142-8555, Japan
SO Annals of the New York Academy of Sciences (**1998**), 865(VIP, PACAP, and Related Peptides), 111-117
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI PACAP protects hippocampal neurons against apoptosis: involvement of **JNK**/SAPK signaling pathway
SO Annals of the New York Academy of Sciences (**1998**), 865(VIP, PACAP, and Related Peptides), 111-117
CODEN: ANYAA9; ISSN: 0077-8923
AB We have demonstrated that the **ischemia**-induced apoptosis of neurons in the CA1 region of the rat hippocampus was prevented by either intracerebroventricular or i.v. infusion of pituitary adenylate cyclase-activating polypeptide (PACAP). However, the mol. mechanisms underlying the anti-apoptotic effect of PACAP remain to be determined Within 3-6 h after **ischemia**, the activities of members of the mitogen-activated protein (MAP) kinase family, including extracellular signal-regulated kinase (ERK), Jun N-terminal kinase (**JNK**)/stress-activated protein kinase (SAPK), and p38 were increased in the hippocampus. The **ischemic** stress had a potent influence on the MAP kinase family, especially on **JNK**/SAPK. PACAP inhibited the activation of **JNK**/SAPK after **ischemic** stress. Secretion of interleukin-6 (IL-6) into the cerebrospinal fluid was intensely stimulated after PACAP infusion. IL-6 inhibited the activation of **JNK**/SAPK, while it activated ERK. These observations suggest that PACAP and IL-6 act to inhibit the **JNK**/SAPK signaling pathway, thereby protecting neurons against apoptosis.
IT Anti-**ischemic** agents
Apoptosis
Signal transduction, biological
(PACAP protects hippocampal neurons against **ischemia**-induced apoptosis and **JNK**/SAPK signaling pathway therein)
IT Cerebrospinal fluid
(PACAP stimulation of interleukin 6 secretion into cerebrospinal fluid in brain **ischemia**-induced apoptosis and **JNK**/SAPK signaling pathway therein)
IT Interleukin 6
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PACAP stimulation of interleukin 6 secretion into cerebrospinal fluid in brain **ischemia**-induced apoptosis and **JNK**/SAPK

signaling pathway therein)
IT Brain
(hippocampus, sector CA1; PACAP protects hippocampal neurons against **ischemia**-induced apoptosis and **JNK**/SAPK signaling pathway therein)
IT Brain, disease
(**ischemia**; PACAP protects hippocampal neurons against **ischemia**-induced apoptosis and **JNK**/SAPK signaling pathway therein)
IT Cytoprotective agents
(neuroprotectants; PACAP protects hippocampal neurons against **ischemia**-induced apoptosis and **JNK**/SAPK signaling pathway therein)
IT 137061-48-4, Pituitary adenylate cyclase-activating peptide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(PACAP protects hippocampal neurons against **ischemia**-induced apoptosis and **JNK**/SAPK signaling pathway therein)
IT 155215-87-5 155215-87-5, Stress-activated protein kinase 165245-96-5, p38 MAP kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PACAP protects hippocampal neurons against **ischemia**-induced apoptosis and **JNK**/SAPK signaling pathway therein)

L6 ANSWER 47 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:64821 CAPLUS
DN 130:149565
TI Mammalian mitogen-activated protein kinase kinase MKK7 isoenzymes and cDNAs and disease treatment
IN Davis, Roger J.; Whitmarsh, Alan; Tournier, Cathy
PA University of Massachusetts, USA
SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9902547	A1	19990121	WO 1998-US14101	19980707 <--
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6136596	A	20001024	US 1997-888429	19970707
	AU 9884778	A1	19990208	AU 1998-84778	19980707 <--
	AU 756143	B2	20030102		
	EP 1005480	A1	20000607	EP 1998-935560	19980707
	R: BE, CH, DE, FR, GB, LI, NL, SE				
	JP 2001509370	T2	20010724	JP 2000-502066	19980707
PRAI	US 1997-888429	A	19970707		
	US 1995-446083	A2	19950519		
	US 1995-530950	A2	19950919		
	WO 1998-US14101	W	19980707		

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
PI WO 9902547 A1 **19990121**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9902547	A1	19990121	WO 1998-US14101	19980707 <--
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

US 6136596	A	20001024	US 1997-888429	19970707	
AU 9884778	A1	19990208	AU 1998-84778	19980707	<--
AU 756143	B2	20030102			
EP 1005480	A1	20000607	EP 1998-935560	19980707	
R: BE, CH, DE, FR, GB, LI, NL, SE					
JP 2001509370	T2	20010724	JP 2000-502066	19980707	

AB Disclosed are human mitogen-activated (MAP) kinase kinase isoforms (MKKs). MKKs mediate unique signal transduction pathways that activate human MAP kinases p38 and **JNK**, which result in activation of other factors, including activating transcription factor-2 (ATF2) and c-Jun. The pathways are activated by a number of factors, including cytokines and environmental stress. Methods are provided for identifying reagents that modulate MKK function or activity and for the use of such reagents in the treatment of MKK-mediated disorders.

ST sequence human mouse MAPK kinase isoenzyme cDNA; mitogen activated MKK7 p38 **JNK** activation; disease treatment mitogen activated kinase MKK7 modulator

IT Heart, disease
(**ischemia**; mammalian mitogen-activated protein kinase kinase MKK7 isoenzymes and cDNAs and disease treatment)

IT 155215-87-5, **JNK** kinase
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(MKK7 substrate; mammalian mitogen-activated protein kinase kinase MKK7 isoenzymes and cDNAs and disease treatment)

L6 ANSWER 48 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:38927 CAPLUS
DN 130:221617
TI Severe cardiomyopathy in mice lacking dystrophin and MyoD
AU Megeney, Lynn A.; Kablar, Boris; Perry, Robert L. S.; Ying, Chuyan; May, Linda; Rudnicki, Michael A.
CS Institute for Molecular Biology and Biotechnology, McMaster University, Hamilton, ON, L8S 4K1, Can.
SO Proceedings of the National Academy of Sciences of the United States of America (**1999**), 96(1), 220-225
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Proceedings of the National Academy of Sciences of the United States of America (**1999**), 96(1), 220-225
CODEN: PNASA6; ISSN: 0027-8424

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**JNK**-1; progression of skeletal muscle damage as contributing factor leading to development of cardiomyopathy in mouse model of Duchenne muscular dystrophy)

IT Heart, disease
(**hypertrophy**; progression of skeletal muscle damage as contributing factor leading to development of cardiomyopathy in mouse model of Duchenne muscular dystrophy)

IT Heart, disease
(**infarction**; progression of skeletal muscle damage as contributing factor leading to development of cardiomyopathy in mouse model of Duchenne muscular dystrophy)

L6 ANSWER 49 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:806931 CAPLUS
DN 130:47550
TI Angiotensin II
AU Kin, Shokei
CS Med. Sch., Osaka City Univ., Osaka, 545, Japan
SO Kekkan to Naihi (**1998**), 8(6), 627-633
CODEN: KENAE5; ISSN: 0917-5318
PB Medikaru Rebyusha
DT Journal; General Review
LA Japanese
SO Kekkan to Naihi (**1998**), 8(6), 627-633
CODEN: KENAE5; ISSN: 0917-5318
AB A review with 15 refs. on activation of protein kinase C, extracellular signal-regulated kinase (ERK), c-jun amino-terminal kinase (**JNK**), protein formation, expression of growth factors, etc., by angiotensin II (AII), activation of ERK and **JNK** after balloon injury, and involvement of AII in hypertension and noninsulin-dependent **diabetes**.
ST review angiotensin II hypertension **diabetes**
IT Hypertension
(activity of angiotensin II and its involvement in hypertension and **diabetes**)
IT **Diabetes** mellitus
(non-insulin-dependent; activity of angiotensin II and its involvement in hypertension and **diabetes**)
IT 11128-99-7, Angiotensin II
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(activity of angiotensin II and its involvement in hypertension and **diabetes**)

L6 ANSWER 50 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:722829 CAPLUS
DN 130:181368
TI Sublytic C5b-9 induces proliferation of human aortic smooth muscle cells. Role of mitogen activated protein kinase and phosphatidylinositol 3-kinase
AU Niculescu, Florin; Badea, Tudor; Rus, Horea
CS Department of Pathology, School of Medicine, University of Maryland, Baltimore, MD, 21201, USA
SO Atherosclerosis (Shannon, Ireland) (**1999**), 142(1), 47-56
CODEN: ATHSBL; ISSN: 0021-9150
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Atherosclerosis (Shannon, Ireland) (**1999**), 142(1), 47-56
CODEN: ATHSBL; ISSN: 0021-9150
AB Proliferation of vascular smooth muscle cells contributes to initial hyperplasia during atherogenesis, but the factors regulating their proliferation are not well known. In the present study we report that sublytic C5b-9 assembly induced proliferation of differentiated human aortic smooth muscle cells (ASMC) in culture. Cell cycle re-entry occurred through activation of cdk4, cdk2 kinase and the reduction of p21 cell cycle inhibitor. We also investigated if C5b-9 cell cycle induction is mediated through activation of mitogen activated protein kinase (MAPK) pathways. Extracellular signal regulated kinase (ERK) 1 activity was significantly increased, while c-jun NH2-terminal kinase (**JNK**) 1 and p38 MAPK activity were only transiently increased. Pretreatment with wortmannin inhibits ERK1 activation by C5b-9, suggesting the involvement of phosphatidylinositol 3-kinase (PI 3-kinase). Both PI 3-kinase and p70

S6 kinase were activated by C5b-9 but not by C5b6. C5b-9 induced DNA synthesis was abolished by pretreatment with inhibitors of ERK1 and PI 3-kinase, but not by p38 MAPK. These data indicated that ERK1 and PI 3-kinase play a major role in C5b-9 induced ASMC proliferation.

ST vascular smooth muscle proliferation C5b9 MAPK phosphatidylinositol kinase **atherosclerosis**

IT **Atherosclerosis**
Cell cycle
Cell proliferation
Hyperplasia
Signal transduction, biological
(sublytic C5b-9 inducing proliferation of human aortic smooth muscle cells and involving ERK1 pathway and phosphatidylinositol 3-kinase)

L6 ANSWER 51 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:680693 CAPLUS
DN 130:79693
TI **Ischemia**/reperfusion injury in the liver of BALB/c mice activates AP-1 and nuclear factor κB independently of IκB degradation
AU Zwacka, Ralf M.; Zhang, Yulong; Zhou, Weihong; Halldorson, Jeff; Engelhardt, John F.
CS Department of Anatomy and Cell Biology, University of Iowa, Iowa City, IA, USA
SO Hepatology (Philadelphia) (**1998**), 28(4), 1022-1030
CODEN: HPTLD9; ISSN: 0270-9139
PB W. B. Saunders Co.
DT Journal
LA English
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Ischemia**/reperfusion injury in the liver of BALB/c mice activates AP-1 and nuclear factor κB independently of IκB degradation
SO Hepatology (Philadelphia) (**1998**), 28(4), 1022-1030
CODEN: HPTLD9; ISSN: 0270-9139

AB For many inherited and acquired hepatic diseases, liver transplantation is the only possible therapeutic strategy. **Ischemia**/reperfusion (I/R) damage to donor tissue is thought to be one component that may play a role in the decline of posttransplant tissue function and ultimately rejection. The transcription factors, AP-1 and nuclear factor κB (NF-κB), play important roles in the acute cellular responses to tissue damage, as well as the inflammatory phase following I/R. The authors have found that the DNA binding activity of AP-1 was dramatically increased following warm **ischemia** at 1 to 3 h postreperfusion. Induced DNA binding activity was composed of predominately c-Jun and JunD hetero- and homodimers as determined by electrophoretic mobility supershift assays. This increase in AP-1 activity occurred in the absence of significant changes in the steady-state protein levels of c-Jun and JunB. Maximal activation of Jun amino-terminal kinase (**JNK**) occurred within the 25 to 30 min postreperfusion, just before the peak in AP-1 DNA binding. These findings suggest that phosphorylation may play an important role in regulating AP-1 transcriptional complexes. Furthermore, JunD protein levels slightly increased at 3 h postreperfusion, concordant with changes in AP-1 DNA binding activity. The activation of NF-κB at 1 h postreperfusion was independent of proteolytic degradation of IκB-α or IκB-β. This activation of NF-κB DNA binding activity in the nucleus was preceded by an increase in tyrosine phosphorylation of IκB-α. These studies suggest that **JNK**, IκB tyrosine kinase, and JunD are potential targets for therapeutic intervention during liver I/R injury.

ST **ischemia** reperfusion injury liver AP1 NFkappaB IkappaB

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1); **ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(IκB (inhibitor of NF-κB); **ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-κB (nuclear factor κB); **ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation)

IT **Transplant** rejection
(allotransplant; **ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation in relation to)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-jun, AP-1 containing; **ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation)

IT Reperfusion
(injury; **ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation)

IT Protein degradation
(**ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation)

IT **Transplant** rejection
(**ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation in relation to)

IT Liver, disease
(**ischemia**; **ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(junD, AP-1 containing; **ischemia**/reperfusion injury in liver of BALB/c mice activates AP-1 and NF-κB independently of IκB degradation)

IT Phosphorylation, biological
(protein; **ischemia**/reperfusion injury in liver of BALB/c mice activates Jun amino-terminal kinase and tyrosine phosphorylation of IκB-α)

IT 155215-87-5, **JNK** kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ischemia**/reperfusion injury in liver of BALB/c mice activates Jun amino-terminal kinase and tyrosine phosphorylation of IκB-α)

IT 60-18-4, L-Tyrosine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(phosphorylation; **ischemia**/reperfusion injury in liver of BALB/c mice activates Jun amino-terminal kinase and tyrosine phosphorylation of IκB-α)

L6 ANSWER 52 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:670081 CAPLUS
DN 130:64578
TI Regulation of myocardial growth and apoptosis by stress kinase signal transduction pathways in neonatal cardiac myocytes
AU Zechner, Dietmar Kurt
CS Univ. of California, San Diego, CA, USA
SO (**1998**) 234 pp. Avail.: UMI, Order No. DA9834975
From: Diss. Abstr. Int., B 1998, 59(5), 1976
DT Dissertation
LA English
SO (**1998**) 234 pp. Avail.: UMI, Order No. DA9834975
From: Diss. Abstr. Int., B 1998, 59(5), 1976
ST stress kinase signaling myocyte neonate cardiac **hypertrophy** apoptosis
IT Heart, disease
(**hypertrophy**; myocardial growth and apoptosis by stress kinase signal transduction pathways regulation in neonatal cardiac myocytes)
IT 155215-87-5, Protein kinase **JNK** 165245-96-5, p38 MAP kinase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(myocardial growth and apoptosis by stress kinase signal transduction pathways regulation in neonatal cardiac myocytes)

L6 ANSWER 53 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:660492 CAPLUS
DN 130:23604
TI Oxidative stress induces DNA fragmentation and caspase activation via the c-Jun NH2-terminal kinase pathway in H9c2 cardiac muscle cells
AU Turner, Neil A.; Xia, Fen; Azhar, Gohar; Zhang, Xiaomin; Liu, Lixin; Wei, Jeanne Y.
CS Gerontology Division, Department of Medicine, Beth Israel-Deaconess Medical Center and the Division on Aging, Harvard Medical School, Boston, MA, 02215, USA
SO Journal of Molecular and Cellular Cardiology (**1998**), 30(9), 1789-1801
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic Press
DT Journal
LA English
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Molecular and Cellular Cardiology (**1998**), 30(9), 1789-1801
CODEN: JMCDAY; ISSN: 0022-2828
AB The aim of this study was to test the hypothesis that oxidative stress induces apoptosis in the H9c2 cardiac muscle cell line, and that signaling via mitogen-activated protein kinase (MAPK) pathways is involved. Three forms of oxidative stress were utilized: the superoxide generator menadione; hydrogen peroxide; or simulated **ischemia** followed by reperfusion. Relatively low concns. of menadione (10 μM) or H2O2 (250 μM) caused maximal DNA fragmentation and caspase activation, both markers for apoptotic cell death, and preferential activation of the c-Jun NH2-terminal kinase (**JNK**) and p38 MAPK pathways. In contrast, higher concns. of menadione or H2O2 caused less DNA fragmentation, more necrotic cell death and preferential activation of the extracellular signal-regulated kinase (ERK) pathway. Simulated **ischemia** alone

did not induce DNA fragmentation or caspase activation and activated only the p38 MAPK pathway. However, **ischemia** plus reperfusion resulted in DNA fragmentation, caspase activation, necrotic cell death and activation of all three MAPK pathways. Selective inhibition of the ERK or p38 MAPK pathways (by PD98059 or SB-203580, resp.) had no effect on the extent of oxidative stress-induced DNA fragmentation or caspase activation. In contrast, inhibition of the **JNK** pathway by transfection of a dominant neg. mutant of **JNK** markedly reduced the extent of DNA fragmentation and caspase activation induced by oxidative stress. In conclusion, these data suggest that the **JNK** pathway plays an important role in signaling oxidative stress-induced apoptosis of H9c2 cardiac muscle cells. (c) 1998 Academic Press.

ST oxidative stress DNA fragmentation caspase **JNK** kinase heart

IT Heart, disease
(**ischemia**; oxidative stress inducing DNA fragmentation and caspase activation via c-Jun NH2-terminal kinase pathway in H9c2 cardiac muscle cells in relation to apoptosis and necrosis and other kinases)

L6 ANSWER 54 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:659918 CAPLUS
DN 130:23599
TI Identification of a novel stress activated kinase in kidney and heart
AU De Silva, Heshani; Cioffi, Catherine; Yin, Tinggui; Sandhu, Gulzar; Webb, Randy L.; Whelan, James
CS Novartis Institute for Biomedical Research, Summit, NJ, 07901, USA
SO Biochemical and Biophysical Research Communications (**1998**), 250(3), 647-652
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Biochemical and Biophysical Research Communications (**1998**), 250(3), 647-652
CODEN: BBRCA9; ISSN: 0006-291X

AB The authors have previously described the patterns of stress kinase activation in rat kidney and heart in response to **ischemia** /reperfusion. During the course of these studies, the authors observed the activation of a novel kinase capable of phosphorylating c-Jun on serines 63 and 73. The mol. weight of this kinase is approx. 37 kDa, significantly below the mol. weight of all previously identified Jun N-terminal kinase (**JNK**) isoforms. The pattern of activation of this 37 kDa kinase in response to **ischemia**/reperfusion in both kidney and heart is distinct from that of known **JNK** isoforms. Western anal. of human renal proximal tubular epithelial (RPTE) cells, using a non-isoform specific phospho-**JNK** antibody, revealed the phosphorylation (activation) of a 37 kDa protein in response to hypoxia. The 37 kDa protein in RPTE cells is phosphorylated by other stress stimuli capable of activating **JNK**. Western anal. of tissues, using a non-isoform specific **JNK** antibody, identifies a cross-reactive 37 kDa protein expressed in the liver, thymus and lymph node which is likely to correspond to the 37 kDa stress-activated kinase. The results of this study have led to the identification of a potentially novel kinase closely related to **JNK** but showing a distinct pattern of activation. (c) 1998 Academic Press.

ST stress activated kinase kidney heart **ischemia** hypoxia

IT Heart, disease
Kidney, disease
(**ischemia**; identification of novel stress activated kinase in human and rat kidney cells and heart and expression in human liver,

thymus, and lymph nodes)

L6 ANSWER 55 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:638181 CAPLUS
DN 130:48189
TI Transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and C/EBPβ; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress
AU Mietus-Snyder, Michele; Glass, Christopher K.; Pitas, Robert E.
CS Gladstone Institute of Cardiovascular Disease and Cardiovascular Research Institute, University of California, San Francisco, CA, 94141-9100, USA
SO Arteriosclerosis, Thrombosis, and Vascular Biology (**1998**), 18(9), 1440-1449
CODEN: ATVBFA; ISSN: 1079-5642
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and C/EBPβ; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress
SO Arteriosclerosis, Thrombosis, and Vascular Biology (**1998**), 18(9), 1440-1449
CODEN: ATVBFA; ISSN: 1079-5642
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1), transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)
IT Genetic element
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(AP-1 site, AP-1/ets composite element; transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-IL6 (nuclear factor interleukin 6), transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)
IT Transcriptional regulation
(activation, transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-jun, transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and

oxidative stress)

IT Scavenger receptors
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(class A (SR-A); transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(for class A scavenger receptor; transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)

IT Muscle
(smooth, transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)

IT Genetic element
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(transcription factor C/EBP-responsive element; transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)

IT Reactive oxygen species
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by oxidative stress)

IT **Atherosclerosis**
Oxidative stress, biological
Signal transduction, biological
(transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)

IT Promoter (genetic element)
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)

IT 217308-51-5
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(C/EBPβ binding element; transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)

IT 141436-78-4, Protein kinase C
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters)

IT 16561-29-8, Phorbol 12-myristate 13-acetate
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

extracellular signal-regulated kinases (ERK), and stress-activated protein kinases (SAPK)/c-Jun N-terminal protein kinases (**JNK**), were determined in protein exts. of the vasculature using protein kinase assay and Western blot anal. After balloon **angioplasty**, ERK2 and JNK1 activities in the vessel wall increased rapidly, reached a high level in 5 min and maintained for 1 h. A sustained increase in ERK2 kinase activity was observed over the next 7 days in the arterial wall and 14 days in neointima after injury. In contrast, opposite and uninjured arteries did not show significant changes in these kinase activities. Concomitantly, Western blot anal. confirmed that the ERK2 kinase in the injured vessels was indeed activated or phosphorylated, showing a slowly migrating species of a 42-kDa protein containing phosphorylated tyrosine. Kinase activation is followed by an increase in c-fos and c-jun gene expression and enhanced activator protein 1 (AP-1) DNA-binding activity. Thus, balloon injury rapidly activates the MAP kinases in rat carotid arteries. These kinase activations may be crucial in mediating smooth muscle cell proliferation in response to vascular **angioplasty**.

ST MAP kinase AP1 artery injury **angioplasty**

IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(AP-1 (activator protein 1); activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

IT **Atherosclerosis**
Cell proliferation
Signal transduction, biological
(activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

IT Artery
(**angioplasty**; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

IT mRNA
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(c-fos and c-jun; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-fos; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

IT Artery
Artery
(coronary, bypass surgery; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

IT Gene
(expression; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

IT Artery, disease
(injury; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

IT Artery
(intima, neointima, formation of; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in

rat carotid arteries after balloon injury)
IT Artery, disease
(**restenosis**; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)
IT Blood vessel
(smooth muscle; activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)
IT 137632-08-7, ERK2 kinase 142243-02-5, Mitogen-activated protein kinase 155215-87-5, JNK1 protein kinase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury)

L6 ANSWER 80 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:801426 CAPLUS
DN 128:87184
TI ErbB kinases and NDF signaling in human prostate cancer cells
AU Grasso, Adam W.; Wen, Duanzhi; Miller, Casey M.; Rhim, Johng S.; Pretlow, Thomas G.; Kung, Hsing-Jien
CS Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, OH, 44106-4960, USA
SO Oncogene (**1997**), 15(22), 2705-2716
CODEN: ONCNES; ISSN: 0950-9232
PB Stockton Press
DT Journal
LA English
RE.CNT 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Oncogene (**1997**), 15(22), 2705-2716
CODEN: ONCNES; ISSN: 0950-9232
AB Prostate carcinoma (PCA) is the most commonly diagnosed malignancy in American men. Our knowledge of PCA growth regulation lags behind that of other cancers, such as breast and colon carcinomas. Among receptor tyrosine kinases, the ErbB family is most frequently implicated in neoplasia. The authors report here the expression of ErbB family kinases and their ligands in PCA cell lines and a xenograft. While ErbB1/EGFR, ErbB2/NEU, and ErbB3 were always observed in a distinct pattern, ErbB4 was not observed Interestingly, while TGF-α was expressed in the majority of PCA lines, the ligand Neu Differentiation Factor/Heregulin (NDF) was expressed only in an immortalized, non-transformed prostate epithelial line. Concomitantly, there was a significant difference in biol. response to these ligands. NDF inhibited LNCaP growth and induced an epithelial-like morphol. change, in contrast to TGF-α, which accelerated cell growth. The authors also performed the first comprehensive anal. of NDF signaling in a prostate line. LNCaP stimulated with NDF demonstrated crosstalk between ErbB3 and ErbB2 which did not involve ErbB1. NDF also turned on several cascades, including those of PI3-K, ERK/MAPK, mHOG/p38 and **JNK**/SAPK, but not those of PLCγ or the STAT family. This signaling pattern is distinct from that of TGF-α. The activation of mHOG by ErbB2 or ErbB3 has not been reported, and may contribute to the unusual phenotype. PI3-K activation is characterized by the formation of a striking "activation complex" with multiple tyrosine-phosphorylated species, including ErbB3. The authors' studies provide a framework in which to dissect the growth and differentiation signals of prostate cancer cells.
IT **Transplant** and Transplantation
(xenotransplant, prostate; ErbB kinases and Neu differentiation factor

signaling in human prostate cancer cells)
IT 79079-06-4, EGF receptor protein kinase 115926-52-8, Phosphatidylinositol 3-kinase 137632-07-6, ERK 1 kinase 137632-07-6 137632-08-7, ERK 2 kinase 137632-08-7 137632-09-8 147014-95-7, Gene erbb3 tyrosine kinase 152743-99-2, c-ErbB-4 Receptor tyrosine kinase 155215-87-5, SAPK/**JNK** kinase 165245-96-5, P38 Kinase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(ErbB kinases and Neu differentiation factor signaling in human prostate cancer cells)

L6 ANSWER 81 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:665472 CAPLUS
DN 127:344358
TI Gα16 mimics vasoconstrictor action to induce smooth muscle α-actin in vascular smooth muscle cells through a Jun-NH2-terminal kinase-dependent pathway
AU Higashita, Ryuji; Li, Liying; Van Putten, Vicki; Yamamura, Yoshitaka; Zarinetchi, Fariba; Heasley, Lynn; Nemenoff, Raphael A.
CS Div. Renal Diseases Hypertension, Dep. Med., Univ. Colorado Health Sci. Center, Denver, CO, 80262, USA
SO Journal of Biological Chemistry (**1997**), 272(41), 25845-25850
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Biological Chemistry (**1997**), 272(41), 25845-25850
CODEN: JBCHA3; ISSN: 0021-9258
AB Prolonged exposure of vascular smooth muscle cells (VSMC) to vasoconstrictors such as vasopressin or angiotensin II induces **hypertrophy** and increases expression of muscle-specific genes including smooth muscle α-actin (SM-α-actin). These vasoconstrictors signal through G-proteins, including members of the Gq family. To further investigate the role of Gq family members, VSMC were transfected with a constitutively active mutant of a Gq family member, Gα16 (Gα16Q212L). Stable expression of Gα16Q212L persistently stimulated phospholipase C, resulting in increased basal levels of inositol phosphates. These cells were hypertrophied and expressed elevated levels of SM-α-actin compared with wild-type VSMC or cells transfected with a control plasmid (NEO). SM-α-actin promoter activity was markedly increased in cells stably or transiently expressing Gα16Q212L. Basal c-Jun-NH2-terminal kinase (**JNK**) activity was increased 3-9-fold in cells stably expressing Gα16Q212L, while basal activity of the p42/44 mitogen-activated protein kinase (ERKs) was unaffected. Transient expression of a kinase inactive **JNK** kinase partially inhibited induction of SM-α-actin promoter activity in response to vasoconstrictors or expression of Gα16Q212L. These results indicate that expression of constitutively active Gα16 in VSMC mimics the effects of vasoconstrictors on **hypertrophy** and muscle-specific gene expression, and activation of **JNK** may play a role in these responses.
ST G16 protein vasoconstriction actin **JNK** kinase
IT 155215-87-5, **JNK** protein kinase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Gα16 mimics vasoconstrictor action to induce smooth muscle α-actin in vascular smooth muscle cells through Jun-NH2-terminal kinase-dependent pathway)

L6 ANSWER 82 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:652925 CAPLUS
DN 127:344732
TI A role for the p38 mitogen-activated protein kinase pathway in myocardial cell growth, sarcomeric organization, and cardiac-specific gene expression
AU Zechner, Dietmar; Thuerauf, Donna J.; Hanford, Deanna S.; Mcdonough, Patrick M.; Glembotski, Christopher C.
CS Department of Biology and Molecular Biology Institute, San Diego State University, San Diego, CA, 92182, USA
SO Journal of Cell Biology (**1997**), 139(1), 115-127
CODEN: JCLBA3; ISSN: 0021-9525
PB Rockefeller University Press
DT Journal
LA English
RE.CNT 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Cell Biology (**1997**), 139(1), 115-127
CODEN: JCLBA3; ISSN: 0021-9525
AB Three hallmark features of the cardiac hypertrophic growth program are increases in cell size, sarcomeric organization, and the induction of certain cardiac-specific genes. All three features of **hypertrophy** are induced in cultured myocardial cells by α1-adrenergic receptor agonists, such as phenylephrine (PE) and other growth factors that activate mitogen-activated protein kinases (MAPKs). In this study the MAPK family members extracellular signal-regulated kinase (ERK), c-jun NH2-terminal kinase (**JNK**), and p38 were activated by transfecting cultured cardiac myocytes with constructs encoding the appropriate kinases possessing gain-of-function mutations. Transfected cells were then analyzed for changes in cell size, sarcomeric organization, and induction of the genes for the A- and B-type natriuretic peptides (NPs), as well as the α-skeletal actin (α-SkA) gene. While activation of **JNK** and/or ERK with MEKK1COOH or Raf-1 BXB, resp., augmented cell size and effected relatively modest increases in NP and α-SkA promoter activities, neither upstream kinase conferred sarcomeric organization. However, transfection with MKK6 (Glu), which specifically activated p38, augmented cell size, induced NP and α-Ska promoter activities by up to 130-fold, and elicited sarcomeric organization in a manner similar to PE. Moreover, all three growth features induced by MKK6 (Glu) or PE were blocked with the p38-specific inhibitor, SB 203580. These results demonstrate novel and potentially central roles for MKK6 and p38 in the regulation of myocardial cell **hypertrophy**.
ST p38 MAP kinase sarcomere cardiac **hypertrophy**; natriuretic peptide p38 kinase cardiac **hypertrophy**; skeletal actin p38 kinase cardiac **hypertrophy**
IT Heart, disease
(**hypertrophy**; role for p38 mitogen-activated protein kinase pathway in myocardial cell growth, sarcomeric organization, and cardiac-specific gene expression)

L6 ANSWER 83 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:561468 CAPLUS
DN 127:218919
TI Transient forebrain **ischemia** in the adult gerbil is associated with a complex c-Jun response
AU Ferrer, Isidro; Ballabriga, Jordi; Pozas, Esther
CS Unitat de Neuropatologia, Servei d'Anatomia Patologica, Hospital Princeps d'Espanya, 08907 Hospitalet de Llobregat, Universitat de Barcelona, Spain
SO NeuroReport (**1997**), 8(11), 2483-2487
CODEN: NERPEZ; ISSN: 0959-4965
PB Rapid Science Publishers

DT Journal
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Transient forebrain **ischemia** in the adult gerbil is associated with a complex c-Jun response
SO NeuroReport (**1997**), 8(11), 2483-2487
CODEN: NERPEZ; ISSN: 0959-4965
AB C-Jun expression in the hippocampus of gerbils subjected to 5 min of transient forebrain **ischemia** was examined with immunohistochem. and western blotting using to c-Jun antibodies raised against two different amino acid sequences. Both c-Jun antibodies showed increased immunoreactivity at 6 and 12 h postischemia in the stratum pyramidale of CA3 and granule cell layer of the dentate gyrus. No immunostaining was detected in CA1 up to the 7th day. Western blots showed increased c-Jun immunoreactivity at 6 and 12 h. However, the antibody c-Jun (AB-1) detected a single band at about p39 in normal and post-**ischemic** states, whereas the antibody c-Jun/AP-1 (N) recognized a band at about p39 in normal and post-**ischemic** gerbils, and a p62 phosphorylated double-band at 6 and 12 h following **ischemia**. In addition, increased c-Jun N-terminal kinase-1 (**JNK**-1) expression was observed on western blots at 6 and 12 h postischemia. These results suggest that different c-Jun-related responses, some of which probably indicate post-translational changes of the c-Jun protein, occur in the hippocampus of the gerbil following transient forebrain **ischemia**.
ST cJun kinase hippocampus transient forebrain **ischemia**
IT Transcription factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(c-jun; c-Jun expression in hippocampus response to transient forebrain **ischemia**)
IT Gene
(expression; c-Jun expression in hippocampus response to transient forebrain **ischemia**)
IT Brain, disease
Brain, disease
(forebrain, **ischemia**, transient; c-Jun expression in hippocampus response to transient forebrain **ischemia**)
IT Brain
(hippocampus; c-Jun expression in hippocampus response to transient forebrain **ischemia**)
IT 155215-87-5, c-Jun N-terminal kinase
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(c-Jun expression in hippocampus response to transient forebrain **ischemia**)

L6 ANSWER 84 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:517828 CAPLUS
DN 127:174591
TI Hypertrophic heart in hypertension and apoptosis
AU Aikawa, Ryuichi; Komuro, Issei
CS Igakubu, Tokyo Daigaku, Tokyo, 113, Japan
SO Kekkan to Naihi (**1997**), 7(4), 370-376
CODEN: KENAE5; ISSN: 0917-5318
PB Medikaru Rebyusha
DT Journal; General Review
LA Japanese
SO Kekkan to Naihi (**1997**), 7(4), 370-376
CODEN: KENAE5; ISSN: 0917-5318
AB A review, with 33 refs., on mol. mechanism of cardiac **hypertrophy** studied using cultured myocardial cells under mech. stretching and

significance of protein kinase C in the signaling, involvement of active O species in the mech. stress-induced apoptosis of cardiomyocytes, humoral factors, e.g. angiotensin II, endothelin-1, etc., in apoptosis, and relation of apoptosis and cardiomyocyte **hypertrophy** by activation of tyrosine kinases, e.g. leukocyte tyrosine kinase (ltk), **JNK**, and p38MAPK. A novel serine/threonine kinase, apoptosis signal kinase 1 (ASK1), and its involvement in signaling pathway of stretching-induced apoptosis of cardiomyocyte is also discussed.

ST review hypertensive cardiac **hypertrophy** apoptosis

IT Heart, disease
(**hypertrophy**; hypertrophic heart in hypertension and apoptosis)

L6 ANSWER 85 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:423012 CAPLUS
DN 127:147817
TI A novel mechanism of JNK1 activation. Nuclear translocation and activation of JNK1 during **ischemia** and reperfusion
AU Mizukami, Yoichi; Yoshioka, Katsuji; Morimoto, Sachio; Yoshida, Ken-ichi
CS Department Legal Medicine, Yamaguchi University School Medicine, Yamaguchi, Japan
SO Journal of Biological Chemistry (**1997**), 272(26), 16657-16662
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
TI A novel mechanism of JNK1 activation. Nuclear translocation and activation of JNK1 during **ischemia** and reperfusion
SO Journal of Biological Chemistry (**1997**), 272(26), 16657-16662
CODEN: JBCHA3; ISSN: 0021-9258
AB Cytokines and various cellular stresses are known to activate c-Jun NH2-terminal kinase (**JNK**), which plays a role in conveying signals from the cytosol to the nucleus. Here, the authors investigate the translocation and activation of JNK1 during **ischemia** and reperfusion in perfused rat heart. **Ischemia** induces the translocation of JNK1 from the cytosol fraction to the nuclear fraction in a time-dependent manner. Immunohistochem. observation also shows that JNK1 staining in the nucleus is enhanced after **ischemia**. During reperfusion after **ischemia**, further nuclear translocation of JNK1 is apparently inhibited. In contrast, JNK1 activity in the nuclear fraction does not increased during **ischemia** but increases during reperfusion with a peak at 10 min of reperfusion. The activation of JNK1 is confirmed by the phosphorylation of endogenous c-Jun (Ser-73) with similar kinetics. The level of c-jun mRNA also increases during reperfusion but not during **ischemia**. Based on fractionation and immunohistochem. analyses, an upstream kinase for JNK1, SAPK/ERK kinase 1 (SEK1), is constantly present in both the nucleus and cytoplasm throughout **ischemia** and reperfusion, whereas an upstream kinase for mitogen-activated protein kinase, MAPK/ERK kinase 1, remains in the cytosol. Furthermore, phosphorylation at Thr-223 of SEK1, necessary for its activation, rapidly increases in the nuclear fraction during postischemic reperfusion. Thus, JNK1 translocates to the nucleus during **ischemia** without activation and is then activated during reperfusion, probably by SEK1 in the nucleus.

ST JNK1 kinase translocation activation heart **ischemia**

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-jun; nuclear translocation and activation of JNK1 during **ischemia** and reperfusion)

IT mRNA
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);

BIOL (Biological study); OCCU (Occurrence)
(gene c-jun; nuclear translocation and activation of JNK1 during **ischemia** and reperfusion)
IT Biological transport
(intracellular; nuclear translocation and activation of JNK1 during **ischemia** and reperfusion)
IT Heart, disease
(**ischemia**; nuclear translocation and activation of JNK1 during **ischemia** and reperfusion)
IT Cell nucleus
Cytoplasm
(nuclear translocation and activation of JNK1 during **ischemia** and reperfusion)
IT Reperfusion
(of **ischemic** heart; nuclear translocation and activation of JNK1 during **ischemia** and reperfusion)
IT 155215-87-5, Gene jnk1 protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nuclear translocation and activation of JNK1 during **ischemia** and reperfusion)
IT 137632-07-6, Protein kinase ERK 1
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(nuclear translocation and activation of JNK1 during **ischemia** and reperfusion)

L6 ANSWER 86 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:356981 CAPLUS
DN 127:93564
TI The MEKK-**JNK** pathway is stimulated by α1-adrenergic receptor and Ras activation and is associated with in vitro and in vivo cardiac **hypertrophy**
AU Ramirez, M. Teresa; Sah, Valerie P.; Zhao, Xiao-Lan; Hunter, John J.; Chien, Kenneth R.; Brown, Joan Heller
CS Department Pharmacology, University California, San Diego, La Jolla, CA, 92093, USA
SO Journal of Biological Chemistry (**1997**), 272(22), 14057-14061
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI The MEKK-**JNK** pathway is stimulated by α1-adrenergic receptor and Ras activation and is associated with in vitro and in vivo cardiac **hypertrophy**
SO Journal of Biological Chemistry (**1997**), 272(22), 14057-14061
CODEN: JBCHA3; ISSN: 0021-9258
AB In neonatal rat ventricular myocytes, stimulation of the α1-adrenergic receptor (α1-AdrR) activates a program of genetic and morphol. changes characterized by transcriptional activation of the atrial natriuretic factor (ANF) gene and enlargement (**hypertrophy**) of the cells. The low mol. weight GTPase Ras has been established as an important regulator of **hypertrophy** both in vitro and in vivo. Ras activates a kinase cascade involving Raf, the mitogen-activated protein kinase kinase (MEK), and the extracellular signal-regulated protein kinase (ERK). However, the extent of involvement of this pathway in regulating hypertrophic responses is controversial. The authors demonstrate here that both α1-AdrR stimulation and Ras

can also activate the c-Jun NH2-terminal kinase (**JNK**) in cardiomyocytes. The α1-AdrR effect on **JNK** occurs through a pathway requiring Ras and MEK kinase (MEKK). A constitutively activated mutant of MEKK that preferentially activates **JNK**, stimulates ANF reporter gene expression, while a dominant neg. MEKK mutant inhibits ANF expression induced by phenylephrine. Furthermore, **JNK** activity is increased in the ventricles of mice overexpressing oncogenic Ras, whereas ERK activity is not. These results suggest that the α1-AdrR mediates ANF gene expression through a Ras-MEKK-**JNK** pathway and that activation of this pathway is associated with in vitro and in vivo **hypertrophy**.

ST cardiac **hypertrophy** adrenoceptor MEKK **JNK** Ras; alphal adrenoceptor cardiac **hypertrophy** signal transduction

IT Transcriptional regulation
(activation; α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT Gene
(expression; α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT Phosphoproteins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene c-raf; α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT Heart, disease
(**hypertrophy**; α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT Ras proteins
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p21c-ras; α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT Heart
Heart
(ventricle, myocyte; α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT Signal transduction, biological
(α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT Adrenoceptors
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α1; α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT 142243-02-5 142805-58-1, Kinase (phosphorylating), mitogen-activated protein kinase 155215-87-5, **JNK** kinase
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT 139691-76-2, Gene c Raf protein kinase
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

IT 85637-73-6, Atriopeptin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α1-adrenergic receptor mediates atrial natriuretic factor gene expression in ventricular myocytes through Ras-MEKK-**JNK** pathway and is associated with in vitro and in vivo cardiac **hypertrophy**)

L6 ANSWER 87 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:333697 CAPLUS
DN 127:3709
TI Reperfusion after liver transplantation in rats differentially activates the mitogen-activated protein kinases
AU Bradham, Cynthia A.; Stachlewitz, Robert F.; Gao, Wenshi; Qian, Ting; Jayadev, Supriya; Jenkins, Gary; Hannun, Yusuf; Lemasters, John J.; Thurman, Ronald G.; Brenner, David A.
CS Departments of Biochemistry and Biophysics, The University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SO Hepatology (Philadelphia) (**1997**), 25(5), 1128-1135
CODEN: HPTLD9; ISSN: 0270-9139
PB Saunders
DT Journal
LA English
RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Hepatology (Philadelphia) (**1997**), 25(5), 1128-1135
CODEN: HPTLD9; ISSN: 0270-9139
AB The injury resulting from cold **ischemia** and warm reperfusion during liver transplantation is a major clin. problem that limits graft success. Kupffer cell activation plays a pivotal role in reperfusion injury, and Kupffer cell products, including free radicals and tumor necrosis factor α (TNF-α), are implicated as damaging agents. However, the second messengers and signaling pathways that are activated by the stress of hepatic **ischemia**/reperfusion remain unknown. The purpose of this study is to assess the activation of the three known vertebrate mitogen activated protein kinase (MAPKs) and the activating protein 1 (AP-1) transcription factor in response to **ischemia** and reperfusion in the transplanted rat liver. There was a potent,

sustained induction of c-jun N-terminal kinase (**JNK**), but not of the related MAPKs extracellular signal-regulated kinases (ERK) or p38, upon reperfusion after transplantation. TNF-α mRNA (mRNA) levels and transcription factors AP-1 and nuclear factor-κB (NF-κB) were induced in the liver after 60 min of reperfusion. Finally, there was an elevation of ceramide, but not diacylglycerol or sphingosine, in the transplanted liver. Ceramide is a second messenger generated by TNF-α treatment and is an activator of **JNK**. Because **JNK** activation preceded the elevations in ceramide and TNF-α mRNA, these results suggest that increased hepatic TNF-α and ceramide may perpetuate **JNK** induction, but that they are not the initiating signals of **JNK** activation during reperfusion injury in the transplanted liver.

ST liver **transplant** reperfusion mitogen protein kinase

IT Transcription factors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(AP-1 (activator protein 1); mitogen activated protein kinase (MAPKs) and activating protein 1 (AP-1) transcription factor response to **ischemia** and reperfusion in transplanted liver)

IT Transcription factors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(NF-κB (nuclear factor κB); mitogen activated protein kinase (MAPKs) and activating protein 1 (AP-1) transcription factor response to **ischemia** and reperfusion in transplanted liver)

IT Reperfusion
(injury; mitogen activated protein kinase (MAPKs) and activating protein 1 (AP-1) transcription factor response to **ischemia** and reperfusion in transplanted liver)

IT **Transplant** and Transplantation
(liver; mitogen activated protein kinase (MAPKs) and activating protein 1 (AP-1) transcription factor response to **ischemia** and reperfusion in transplanted liver)

IT Second messenger system
Transplant and Transplantation
(mitogen activated protein kinase (MAPKs) and activating protein 1 (AP-1) transcription factor response to **ischemia** and reperfusion in transplanted liver)

IT Ceramides
Tumor necrosis factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(mitogen activated protein kinase (MAPKs) and activating protein 1 (AP-1) transcription factor response to **ischemia** and reperfusion in transplanted liver)

IT Liver
(**transplant**; mitogen activated protein kinase (MAPKs) and activating protein 1 (AP-1) transcription factor response to **ischemia** and reperfusion in transplanted liver)

IT 142243-02-5, Mitogen activated protein kinase 155215-87-5
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(mitogen activated protein kinase (MAPKs) and activating protein 1 (AP-1) transcription factor response to **ischemia** and reperfusion in transplanted liver)

L6 ANSWER 88 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:221477 CAPLUS

DN 126:301626
TI N-acetyl cysteine ameliorates **ischemic** renal failure
AU DiMari, John; Megyesi, Judit; Udvarhelyi, Nora; Price, Peter; Davis, Roger; Safirstein, Robert
CS Univ. Texas Med. Branch at Galveston, Galveston, TX, 77555-0562, USA
SO American Journal of Physiology (**1997**), 272(3, Pt. 2), F292-F298
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI N-acetyl cysteine ameliorates **ischemic** renal failure
SO American Journal of Physiology (**1997**), 272(3, Pt. 2), F292-F298
CODEN: AJPHAP; ISSN: 0002-9513
AB Recovery from **ischemic** renal injury is accompanied by enhanced DNA synthesis and a typical immediate early (IE) gene response. These two processes occur in distinct cell populations, suggesting that the IE gene response does not serve a proliferative function directly. As cellular stress induces an IE response through activation of the stress-activated protein kinases (SAPK) that is not proliferative and can be inhibited by N-acetyl-L-cysteine (NAC), we determined whether the Jun NH2-terminal kinases (**JNK**), members of the SAPKs, are activated during **ischemia** and whether NAC administration reduces the IE response and/or the induction of **JNK** activity. NAC (6 mM/kg body wt) infused 1 h prior to and 1 h following renal **ischemia** reduced c-fos and c-jun expression by 50 and 70%, resp. **Ischemia** increased **JNK** activity, and this increase was inhibited by NAC. NAC infused animals had a higher glomerular filtration rate at 1 day (NAC, 0.9 ± 0.2, vs. control, 0.05 ± 0.01 mL/min, $P < 0.001$) and 7 days (NAC, 2.0 ± 0.1, vs. control. 1.2 ± 0.1, $P < 0.001$) after the induction of **ischemia**. NAC did not reduce the extent of proximal tubule necrosis at 24 h after reperfusion but improved histol. appearance of the kidney at 7 days. The mechanism by which NAC ameliorates the loss of renal function is unknown but may involve its general properties as an antioxidant or a possible interaction with NAC and NO. We conclude that the IE gene response of the kidney to **ischemia** reperfusion is a consequence of the stress-activated kinase pathway and that part of the response is deleterious to kidney function and cellular integrity.
ST kidney **ischemia** reperfusion stress activated kinase; antiischemic N acetyl cysteine kidney
IT Anti-**ischemic** agents
Reperfusion
(N-acetyl cysteine ameliorates **ischemic** renal failure)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-fos; N-acetyl cysteine ameliorates **ischemic** renal failure)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-jun; N-acetyl cysteine ameliorates **ischemic** renal failure)
IT Kidney, disease
(**ischemia**; N-acetyl cysteine ameliorates **ischemic** renal failure)
IT 616-91-1, N-Acetyl cysteine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-acetyl cysteine ameliorates **ischemic** renal failure)
IT 155215-87-5, Jun NH2-terminal kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(N-acetyl cysteine ameliorates **ischemic** renal failure)

L6 ANSWER 89 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:143027 CAPLUS
DN 126:236631
TI Hypoxia/reoxygenation stimulates Jun kinase activity through redox signaling in cardiac myocytes
AU Laderoute, Keith R.; Webster, Keith A.
CS Department of Cell and Molecular Biology, SRI International, Menlo Park, CA, USA
SO Circulation Research (**1997**), 80(3), 336-344
CODEN: CIRUAL; ISSN: 0009-7330
PB American Heart Association
DT Journal
LA English
SO Circulation Research (**1997**), 80(3), 336-344
CODEN: CIRUAL; ISSN: 0009-7330
AB Hypoxia and reoxygenation are principal components of myocardial **ischemia** and reperfusion and have distinctive effects on the tissue. Both conditions have been associated with inflammation, necrosis, apoptosis, and myocardial **infarction**. Using a cell culture model of **ischemia** and reperfusion in which cardiac myocytes were exposed to cycles of hypoxia and reoxygenation, we report here that reoxygenation, but not hypoxia alone, caused sustained ≈10-fold increases in phosphorylation of the amino-terminal domain of the c-jun transcription factor. The activation was similar to treatments with anisomycin or okadaic acid and correlated with the hypoxia-mediated depression of intracellular glutathione. Reoxygenation-induced c-Jun kinase activity was reduced by preincubating myocytes during the hypoxia phase with the spin-trap agent α-Ph N-tert-butylnitrone or with N-acetylcysteine. The kinase activation was also inhibited by the tyrosine kinase inhibitor genistein but not by other protein kinase inhibitors. These results implicate unquenched reactive oxygen intermediates as the stimulus that initiates a kinase pathway involving the stress-activated protein kinases (JNKs/SAPKs) in reoxygenated cardiac myocytes.
ST hypoxia reoxygenation Jun kinase signaling heart; **JNK** SAPK activation reoxygenation cardiomyocyte

L6 ANSWER 90 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:82022 CAPLUS
DN 126:156387
TI Stress-signaling kinase Sek1 protects thymocytes from apoptosis mediated by CD95 and CD3
AU Nishina, Hiroshi; Fischer, Klaus D.; Radvanyl, Laszlo; Shahinian, Arda; Hakem, Razqallah; Rubie, Elizabeth A.; Bernstein, Alan; Mak, Tak W.; Woodgett, James R.; Penninger, Josef M.
CS Ontario Cancer Inst., Univ. Toronto, Toronto, ON, M5G 2C1, Can.
SO Nature (London) (**1997**), 385(6614), 350-353
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
SO Nature (London) (**1997**), 385(6614), 350-353
CODEN: NATUAS; ISSN: 0028-0836
AB Distinct and evolutionarily conserved signal transduction cascades mediate survival or death in response to developmental and environmental cues. The stress-activated protein kinases, or Jun N-terminal kinases (SAPKs/JNKs), are activated in response to a variety of cellular stresses such as changes in osmolarity and metabolism, DNA damage, heat shock, **ischemia**, or inflammatory cytokines. Sek1 (JNKK/MKK4) is a direct

activator of SAPKs/JNKs in response to environmental stresses or mitogenic factors. Here the authors investigate the role of Sek1 in development and apoptosis by deleting sek1 in embryonic stem (ES) cells by homologous recombination. The authors provide genetic evidence that different stresses utilize distinct signaling pathways for SAPK/**JNK** activation. Sek1-/-/rag2-/- chimeric mice have normal nos. of mature T cells but fewer immature CD4+CD8+ thymocytes. The sek1 mutation did not affect the induction of apoptosis in response to environmental stresses in ES and T cells: instead, sek1 protected thymocytes from CD95 (Fas)- and CD3-mediated apoptosis. These data indicate that SEK1 mediates survival signals in T-cell development.

L6 ANSWER 91 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:67334 CAPLUS
DN 126:71211
TI Cloning of cDNA for cytokine-, stress-, and oncoprotein-activated human protein kinase kinases and their clinical applications
IN Davis, Roger J.; Gupta, Shashi; Raingeaud, Joel; Derijard, Benoit
PA Davis, Roger J., USA; Gupta, Shashi; Raingeaud, Joel; Derijard, Benoit
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9636642	A1	19961121	WO 1996-US1078	19960126	<--
	W: AU, CA, JP, KR, MX					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5804427	A	19980908	US 1995-446083	19950519	<--
	US 5736381	A	19980407	US 1995-530950	19950919	<--
	AU 9649046	A1	19961129	AU 1996-49046	19960126	<--
	AU 710877	B2	19990930			
	EP 830374	A1	19980325	EP 1996-905233	19960126	<--
	EP 830374	B1	20020717			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE					
	JP 2002503946	T2	20020205	JP 1996-534787	19960126	
	AT 220719	E	20020815	AT 1996-905233	19960126	
PRAI	US 1995-446083	A	19950519			
	US 1995-530950	A	19950919			
	WO 1996-US1078	W	19960126			

PI WO 9636642 A1 **19961121**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9636642	A1	19961121	WO 1996-US1078	19960126	<--
	W: AU, CA, JP, KR, MX					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5804427	A	19980908	US 1995-446083	19950519	<--
	US 5736381	A	19980407	US 1995-530950	19950919	<--
	AU 9649046	A1	19961129	AU 1996-49046	19960126	<--
	AU 710877	B2	19990930			
	EP 830374	A1	19980325	EP 1996-905233	19960126	<--
	EP 830374	B1	20020717			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE					
	JP 2002503946	T2	20020205	JP 1996-534787	19960126	
	AT 220719	E	20020815	AT 1996-905233	19960126	

AB Disclosed are the cDNA encoding human mitogen-activated (MAP) kinase kinase isoforms (MKKs) MKK3, MKK4-α, MKK4-β, MKK4γ (all from brain), and MKK6 (from skeletal muscle). MKKs mediate unique signal transduction pathways that activate human MAP kinases p38 and **JNK**, which result in activation of other factors, including activating transcription factor-2 (ATF2) and c-Jun. The pathways are activated by a

number of factors, including cytokines and environmental stress. Methods are provided for identifying reagents that modulate MKK function or activity and for the use of such reagents in the treatment of MKK-mediated disorders consisting of **ischemic** heart failure, kidney failure, etc.

L6 ANSWER 92 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:55211 CAPLUS
DN 126:88170
TI The stress-activated C-Jun protein kinase (**JNK**) is stimulated by lipoxygenase pathway product 12-HETE in RIN m5F cells
AU Bleich, David; Chen, Songyuan; Wen, Yeshao; Nadler, Jerry L.
CS Div. Diabetes, Endocrinol. Metab., City Hope Natl. Med. Cent., Duarte, CA, 91010, USA
SO Biochemical and Biophysical Research Communications (**1997**), 230(2), 448-451
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI The stress-activated C-Jun protein kinase (**JNK**) is stimulated by lipoxygenase pathway product 12-HETE in RIN m5F cells
SO Biochemical and Biophysical Research Communications (**1997**), 230(2), 448-451
CODEN: BBRCA9; ISSN: 0006-291X
AB Cytokine induced pancreatic β-cell destruction seen in Type 1 **diabetes** and islet graft rejection involves multiple intracellular signaling pathways that directly or indirectly lead to inflammatory damage or programmed cell death. IL-1β has been shown to stimulate the 12-lipoxygenase pathway product 12-HETE, in RIN m5F cells; however, the precise role of 12-LO activation in mediating cytokine effects is not clear. Since the stress-activated protein kinase, **JNK**, has been linked to cytokine mediated inflammatory actions, we studied the effect of two LO products, 12-HETE and 15-HETE, on **JNK** activity. We demonstrate that 1 nM 12-HETE stimulates **JNK** activity, while 1 nM 15-HETE, the 15-lipoxygenase pathway product, does not. These results suggest 12-HETE is a novel upstream signal for IL-1β induced **JNK** activation in RIN m5F cells.
ST interleukin HETE **JNK** kinase islet cell
IT Signal transduction, biological
(12-HETE is an upstream signal for interleukin-1β induced **JNK** activation in pancreatic β-cells)
IT Interleukin 1β
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(12-HETE is an upstream signal for interleukin-1β induced **JNK** activation in pancreatic β-cells)
IT Pancreatic islet of Langerhans
(β-cell; 12-HETE is an upstream signal for interleukin-1β induced **JNK** activation in pancreatic β-cells)
IT 54397-83-0, 12-Hete 82391-43-3, 12-Lipoxygenase 155215-87-5, **Jnk** protein kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(12-HETE is an upstream signal for interleukin-1β induced **JNK** activation in pancreatic β-cells)

L6 ANSWER 93 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:10842 CAPLUS
DN 126:99784

TI Angiotensin II stimulates c-Jun NH2-terminal kinase in cultured cardiac myocytes of neonatal rats
AU Kudoh, Sumiyo; Komuro, Issei; Mizuno, Takehiko; Yamazaki, Tsutomu; Zou, Younzeng; Shiojima, Ichiro; Takekoshi, Noboru; Yazaki, Yoshio
CS Dep. Medicine III, Univ. Tokyo, School Medicine, Tokyo, Japan
SO Circulation Research (**1997**), 80(1), 139-146
CODEN: CIRUAL; ISSN: 0009-7330
PB American Heart Association
DT Journal
LA English
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Circulation Research (**1997**), 80(1), 139-146
CODEN: CIRUAL; ISSN: 0009-7330
AB Many lines of evidence have suggested that angiotensin II (Ang II) plays an important role in cardiac **hypertrophy**. Ang II not only increases protein synthesis but also induces the reprogramming of gene expression in cultured cardiac myocytes. In the present study, to elucidate the mechanism by which Ang II regulates gene expression in cardiac myocytes, the authors examined whether Ang II activates c-Jun N-terminal kinase (**JNK**), which is a member of the mitogen-activated protein kinase family and activates the transcription factor, activator protein-1 (AP-1). The activity of **JNK** increased 5 min after the addition of Ang II, peaked at 20 min, and gradually decreased thereafter. Examination of the Ang II dose-response relation revealed detectable **JNK** activation at 10-9 M and maximal activation at 10-6 M. Ang II activated **JNK** through the AT1 receptor, and the activation was attenuated by the downregulation of protein kinase C or the chelation of intracellular Ca2+. Although the addition of either Ca2+ ionophore or phorbol ester resulted in little or no activation of **JNK**, simultaneous addition of both Ca2+ ionophore and phorbol ester markedly activated **JNK**. Slight expressions of the c-jun gene were observed in unstimulated cardiac myocytes, and Ang II increased expressions of the c-jun gene as well as the c-fos gene. Ang II increased transcription of the endothelin-1 gene through the AP-1 binding site. In conclusion, Ang II may activate **JNK** in cultured cardiac myocytes through an increase in intracellular Ca2+ and activation of protein kinase C, and the activated **JNK** may regulate gene expression by activating AP-1 during Ang II-induced cardiac **hypertrophy**.
IT Heart, disease
(**hypertrophy**; angiotensin II stimulates c-Jun NH2-terminal kinase in cultured cardiac myocytes of neonatal rats)
IT 7440-70-2, Calcium, biological studies 141436-78-4, Protein kinase C 155215-87-5, Protein kinase **JNK**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(angiotensin II stimulates c-Jun NH2-terminal kinase in cultured cardiac myocytes of neonatal rats)

L6 ANSWER 94 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:726896 CAPLUS
DN 126:45794
TI The MAP kinase cascades are activated during post-**ischemic** liver reperfusion
AU Bendinelli, Paola; Piccoletti, Roberta; Maroni, Paola; Bernelli-Zazzera, Aldo
CS Istituto di Patologia Generale dell'Universita degli Studi di Milano, Centro di Studio sulla Patologia Cellulare del CNR, Via Mangiagalli 31, Milan, 20133, Italy
SO FEBS Letters (**1996**), 398(2,3), 193-197
CODEN: FEBLAL; ISSN: 0014-5793

PB Elsevier
DT Journal
LA English
TI The MAP kinase cascades are activated during post-**ischemic** liver reperfusion
SO FEBS Letters (**1996**), 398(2,3), 193-197
CODEN: FEBLAL; ISSN: 0014-5793
AB The authors have investigated the involvement of MAP kinase cascades in the response of the liver to post-**ischemic** reperfusion. Both JNKs and ERKs are activated but the duration and magnitude of the increase in their activities appear to be different. **JNK** activation is more marked but shorter than that of ERKs. The increase observed in the phosphotyrosine content of the 52 kDa Shc protein, accompanied by an increased amount of co-immunopptd. Grb2, and the activation of Raf-1 kinase provide evidence of the involvement of a Ras-Raf-dependent pathway, with a time course that is similar to that of ERK activation. The treatment of rats with IL-1 receptor antagonist modified all of the described effects, suggesting that IL-1 plays a role in the response of the liver to reperfusion.
ST MAP kinase liver **ischemia** reperfusion
IT Proteins, specific or class
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Grb-2; MAP kinase cascade activation during post-**ischemic** liver reperfusion)
IT Reperfusion
Signal transduction, biological
(MAP kinase cascade activation during post-**ischemic** liver reperfusion)
IT Interleukin 1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MAP kinase cascade activation during post-**ischemic** liver reperfusion in relation to)
IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SHC; MAP kinase cascade activation during post-**ischemic** liver reperfusion)
IT Liver, disease
(**ischemia**; MAP kinase cascade activation during post-**ischemic** liver reperfusion)
IT 137632-07-6, ERK1 kinase 137632-08-7, ERK2 kinase 139691-76-2, Gene raf-1 kinase 155215-87-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MAP kinase cascade activation during post-**ischemic** liver reperfusion)
IT 142243-02-5, Kinase (phosphorylating), mitogen-activated protein
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(MAP kinase cascades are activated during post-**ischemic** liver reperfusion)

L6 ANSWER 95 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:692718 CAPLUS
DN 126:5892
TI Initiation of acute phase response and synthesis of cytokines
AU Koj, Aleksander
CS Institute of Molecular Biology, Jagiellonian University, Al. Mickiewicza 3, Krakow, 31-120, Pol.

SO Biochimica et Biophysica Acta (**1996**), 1317(2), 84-94
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier
DT Journal; General Review
LA English
SO Biochimica et Biophysica Acta (**1996**), 1317(2), 84-94
CODEN: BBACAQ; ISSN: 0006-3002
AB A review, with 121 refs. A variety of injuries, such as bacterial infection or **ischemic** tissue necrosis, induce systemic acute phase reaction expressed as fever, leukocytosis, release of several hormones, activation of clotting, complement and kinin forming pathways, and drastic increase of synthesis of certain plasma proteins. The reaction is triggered by 'alarm mols.', including free radicals, which activate several stress-sensitive protein kinases (ERK, p38, **JNK**) in macrophages and other responsive cells. These kinases phosphorylate, usually in a multi-step cascade, transcription factors belonging primarily to C/EBP, NF-κB and AP-1 families. Active transcription factors after translocation to nucleus interact with responsive elements in the gene promoters of acute-phase cytokines: tumor necrosis factor-α, interleukin-1 and interleukin-6. Enhanced transcription of these genes is usually followed by rapid translation and precursor protein processing leading to the release of biol. active cytokines. Fine tuning of the acute phase response appears to be regulated at all stages: primary signals, kinase cascades, transcription factors, mRNA stability and translation, cytokine precursor processing, secretion and bioavailability. This makes possible designing of specific inhibitors of cytokine synthesis as potential therapeutic drugs.

L6 ANSWER 96 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:639968 CAPLUS
DN 125:323894
TI The Ras-**JNK** pathway is involved in shear-induced gene expression
AU Li, Yi-Shuan; Shyy, John Y.-J.; Li, Song; Lee, Jongdale; Su, Bing; Karin, Michael; Chien, Shu
CS Institute for Biomedical Engineering, University of California, San Diego, La Jolla, CA, 92093, USA
SO Molecular and Cellular Biology (**1996**), 16(11), 5947-5954
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
TI The Ras-**JNK** pathway is involved in shear-induced gene expression
SO Molecular and Cellular Biology (**1996**), 16(11), 5947-5954
CODEN: MCEBD4; ISSN: 0270-7306
AB Hemodynamic forces play a key role in inducing **atherosclerosis** -implicated gene expression in vascular endothelial cells. To elucidate the signal transduction pathway leading to such gene expression, the effects of fluid shearing on the activities of upstream signaling mols. were studied. Fluid shearing (shear stress, 12 dynes/cm2 [1 dyne = 10-5 N]) induced a transient and rapid activation of p21ras and preferentially activated c-Jun NH2 terminal kinases (JNK1 and JNK2) over extracellular signal-regulated kinases (ERK-1 and ERK-2). Cotransfection of RasN17, a dominant neg. mutant of Ha-Ras, attenuated the shear-activated **JNK** and luciferase reporters driven by 12-O-tetradecanoylphorbol-13-acetate-responsive elements. **JNK**(K-R) and MEKK(K-M), the resp. catalytically inactive mutants of JNK1 and MEKK, also partially inhibited the shear-induced luciferase reporters. In contrast, Raf301, ERK(K71R), and ERK(K52R), the dominant neg. mutants of Raf-1, ERK-1, and ERK-2, resp., had little effect on the activities of these reporters. The activation of **JNK** was also correlated with increased c-Jun transcriptional activity, which was attenuated by a neg. mutant of Son of sevenless. Thus, mech. stimulation exerted by fluid shearing activities

primarily the Ras-MEKK-**JNK** pathway in inducing endothelial gene expression.

ST shear stress Ras MEKK **JNK** pathway

IT Signal transduction, biological
(Ras-**JNK** pathway is involved in shear-induced gene expression)

IT Blood vessel
(endothelium, Ras-**JNK** pathway is involved in shear-induced gene expression)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p21ras, p21 ras; Ras-**JNK** pathway is involved in shear-induced gene expression)

IT Shear
(stress, Ras-**JNK** pathway is involved in shear-induced gene expression)

IT 9014-00-0, Luciferase 146702-84-3, Protein kinase, MEKK 155215-87-5, JNK1 kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Ras-**JNK** pathway is involved in shear-induced gene expression)

L6 ANSWER 97 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:637767 CAPLUS

DN 125:318601

TI Angiotensin II stimulates c-Jun NH2-terminal kinase in cultured cardiac myocytes

AU Kudo, Sumiyo; Komuro, Issei; Takekosi, Noboru

CS Dep. of Cardiology, Kanazawa Medical Univ., Ishikawa, 920-02, Japan

SO Kanazawa Ika Daigaku Zasshi (**1996**), 21(2), 179-187
CODEN: KIDZDN; ISSN: 0385-5759

PB Kanazawa Ika Daigaku Shuppan Kyoku

DT Journal

LA English

SO Kanazawa Ika Daigaku Zasshi (**1996**), 21(2), 179-187
CODEN: KIDZDN; ISSN: 0385-5759

AB Many lines of evidence have suggested that angiotensin II (AII) plays an important role in cardiac **hypertrophy**. All not only increases protein synthesis but also induces the reprogramming of gene expression in cultured cardiac myocytes. In the present study, to elucidate the mechanism by which AII regulates gene expression in cardiac myocytes, we examined whether AII activates c-Jun NH2-terminal kinase (**JNK**), which is a subfamily of the extra acellular signal-regulated kinases (ERKs) group and increases activity of the transcription factor, AP-1. The activity of **JNK** was increased from 5 min after the addition of AII, peaked at 20 min and decreased thereafter. Examination of the AII dose response revealed detectable **JNK** activation at higher concentration than 10-9 M. AII activated **JNK** through AII Type 1 receptor and the activation was attenuated by the down regulation of protein kinase C or chelation of intracellular Ca2+. Although both Ca2+ ionophore and phorbol ester activated ERKs, each stimulus resulted in little or no activation of **JNK**. When both Ca2+ ionophore and phorbol ester were added at the same time, however, **JNK** was markedly activated. AII induced expressions of immediate early response genes such as c-fos and c-jun and increased the activity of AP-1. In conclusion, AII may activate **JNK** in cardiac myocytes through an increase in intracellular Ca2+ and activation of protein kinase C. The activated **JNK** may regulate gene expression during AII-induced cardiac **hypertrophy**.

L6 ANSWER 98 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:478179 CAPLUS
DN 125:161306
TI Stimulation of the stress-activated mitogen-activated protein kinase subfamilies in perfused heart. p38/RK mitogen-activated protein kinases and c-Jun N-terminal kinases are activated by **Ischemia** /reperfusion
AU Bogoyevitch, Marie A.; Gillespie-Brown, Judith; Ketterman, Albert J.; Fuller, Stephen J.; Ben-Levy, Rachel; Ashworth, Alan; Marshall, Christopher J.; Sugden, Peter H.
CS National Heart Lung Institute, Imperial College Science, UK
SO Circulation Research (**1996**), 79(2), 162-173
CODEN: CIRUAL; ISSN: 0009-7330
PB American Heart Association
DT Journal
LA English
TI Stimulation of the stress-activated mitogen-activated protein kinase subfamilies in perfused heart. p38/RK mitogen-activated protein kinases and c-Jun N-terminal kinases are activated by **Ischemia** /reperfusion
SO Circulation Research (**1996**), 79(2), 162-173
CODEN: CIRUAL; ISSN: 0009-7330
AB It has recently been recognized that cellular stresses activate certain members of the mitogen-activated protein kinase (MAPK) superfamily. One role of these "stress-activated" MAPKs is to increase the transactivating activity of the transcription factors c-Jun, Elk1, and ATF2. These findings may be particularly relevant to hearts that have been exposed to pathol. stresses. Using the isolated perfused rat heart, the authors show that global **ischemia** does not activate the 42- and 44kD extracellular signal-regulated (protein) kinase (ERK) subfamily of MAPKs but rather stimulates a 38-kD activator of MPAK-activated protein kinase-2 (MAPKAPK2). This activation is maintained during reperfusion. The mol. characteristics of this protein kinase suggest that it is a member of the p38/reactivating kinase (RK) group of stress-activated MAPKs. In contrast, stress-activated MAPKs of the c-Jun N-terminal kinase (**JNK**/Sapks) subfamily are not activated by **ischemia** alone but are activated by reperfusion following **ischemia**. Furthermore, transfection of ventricular myocytes with activated protein kinases (MEKK1 and SEK1) that may be involved in the upstream activation of **JNK**/SAPKs induces increases in myocyte size and transcriptional changes typical of the hypertrophic response. The authors speculate that activation of multiple parallel MAPK pathways may be important in the responses of hearts to cellular stresses.
ST stress MAPK kinase activation perfusion heart; p38RK MAPK kinase **ischemia** reperfusion activation; cJun kinase **ischemia** reperfusion activation MEKK1; SEK1 MEKK1 cell size promoter activation
IT **Ischemia**
Phosphorylation, biological
Stress, biological
(activation of multiple parallel MAPK pathways may be important in responses of hearts to cellular stresses)

L6 ANSWER 99 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:127606 CAPLUS
DN 124:199413
TI Acute hypertension activates mitogen-activated protein kinases in arterial wall
AU Xu, Qingbo; Liu, Yusen; Gorospe, Myriam; Udelsman, Robert; Holbrook, Nikki J.
CS National Institute on Aging, National Institutes of Health, Baltimore, MD, 21224, USA

SO Journal of Clinical Investigation (**1996**), 97(2), 508-14
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
SO Journal of Clinical Investigation (**1996**), 97(2), 508-14
CODEN: JCINAO; ISSN: 0021-9738
AB Mitogen-activated protein (MAP) kinases are rapidly activated in cells stimulated with various extracellular signals by dual phosphorylation of tyrosine and threonine residues. They are thought to play a pivotal role in transmitting transmembrane signals required for cell growth and differentiation. Herein we provide evidence that two distinct classes of MAP kinases, the extracellular signal-regulated kinases (ERK) and the c-Jun NH2-terminal kinases (**JNK**), are transiently activated in rat arteries (aorta, carotid and femoral arteries) in response to an acute elevation in blood pressure induced by either restraint or administration of hypertensive agents (i.e., phenylephrine and angiotensin II). Kinase activation is followed by an increase in c-fos and c-jun gene expression and enhanced activating protein 1 (AP-1) DNA-binding activity. Activation of ERK and **JNK** could contribute to smooth muscle cell **hypertrophy**/hyperplasia during arterial remodeling due to frequent and/or persistent elevations in blood pressure.
ST ENK **JNK** MAP kinase artery hypertension
IT Hypertension
Transcription, genetic
(ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT Ribonucleic acid formation factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1), ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT Artery
(aorta, ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-fos, ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-jun, ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT Artery
(carotid, ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT Artery
(femoral, ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pp42mapk, ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT 11128-99-7, Angiotensin II
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)
IT 137632-08-7, ERK2 protein kinase 155215-87-5, JNK1 protein kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(ERK and **JNK** mitogen-activated protein kinases response to acute hypertension in arterial wall)

L6 ANSWER 100 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:51820 CAPLUS
DN 124:114234
TI Stimulation of c-Jun kinase and mitogen-activated protein kinase by **ischemia** and reperfusion in the perfused rat heart
AU Knight, Richard J.; Buxton, Denis B.
CS Department Molecular Medical Pharmacology, UCLA School Medicine, Los Angeles, CA, 90095-6948, USA
SO Biochemical and Biophysical Research Communications (**1996**), 218(1), 83-8
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
TI Stimulation of c-Jun kinase and mitogen-activated protein kinase by **ischemia** and reperfusion in the perfused rat heart
SO Biochemical and Biophysical Research Communications (**1996**), 218(1), 83-8
CODEN: BBRCA9; ISSN: 0006-291X
AB **Ischemia** and reperfusion lead to the rapid induction of proto-oncogenes in the heart and subsequent induction of genes with cardioprotective functions. The activity of the transcription factors c-Jun and ATF-2 can be stimulated by activation of c-Jun amino-terminal kinase (**JNK**) in response to a variety of stresses. Here the authors show that **ischemia** and reperfusion led to the activation of **JNK** and also of the distantly-related mitogen activated protein kinase (MAPK). Activation of **JNK**, but not (MAPK), was abolished by removal of calcium from the perfusate immediately prior to **ischemia**. In contrast, infusion of the hydrogen peroxide scavenger catalase abolished activation of MAPK in response to **ischemia** and reperfusion, but activation of **JNK** was inhibited significantly by catalase only when superoxide dismutase was also present. Hydrogen peroxide infusion activated MAPK but not **JNK**, supporting a role for hydrogen peroxide produced during reperfusion in MAPK activation. The authors conclude that while **ischemia** and reperfusion activate both **JNK** and MAPK, the mechanisms of activation are different for the 2 kinases. Activation of these kinases is likely to contribute to altered gene expression in response to **ischemia** and reperfusion.
ST Jun kinase **ischemia** reperfusion heart; MAP kinase heart **ischemia** reperfusion
IT Signal transduction, biological
(reactive oxygen-mediated stimulation of c-Jun kinase and mitogen-activated protein kinase in heart **ischemia** /reperfusion)
IT Heart, disease
(**ischemia**, reactive oxygen-mediated stimulation of c-Jun kinase and mitogen-activated protein kinase in heart **ischemia** /reperfusion)
IT Perfusion
(re-, reactive oxygen-mediated stimulation of c-Jun kinase and mitogen-activated protein kinase in heart **ischemia** /reperfusion)
IT 7722-84-1, Hydrogen peroxide, biological studies 11062-77-4, Superoxide 142243-02-5, Mitogen activated protein kinase 155215-87-5, c-Jun amino-terminal kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(reactive oxygen-mediated stimulation of c-Jun kinase and

mitogen-activated protein kinase in heart **ischemia**
/reperfusion)

IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(reactive oxygen-mediated stimulation of c-Jun kinase in heart **ischemia**/reperfusion is dependent on)

L6 ANSWER 101 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:543568 CAPLUS
DN 122:285539
TI A serine/threonine protein kinase that phosphorylates the N-terminal activation domain of the c-jun protein
IN Karin, Michael; Davis, Roger; Hibi, Masahiko; Lin, Anning; Derijard, Benoit
PA University of California, USA; University of Massachusetts
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9503323	A1	19950202	WO 1994-US8119	19940718	<--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5534426	A	19960709	US 1993-94533	19930719	<--
	US 6514745	B1	20030204	US 1994-220602	19940325	
	AU 9473380	A1	19950220	AU 1994-73380	19940718	<--
	AU 700137	B2	19981224			
	EP 726908	A1	19960821	EP 1994-923544	19940718	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	JP 09507384	T2	19970729	JP 1995-505262	19940718	<--
	JP 2925740	B2	19990728			
	CA 2166981	C	20001107	CA 1994-2166981	19940718	
PRAI	US 1993-94533	A	19930719			
	US 1994-220602	A	19940325			
	WO 1994-US8119	W	19940718			

PI WO 9503323 A1 **19950202**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9503323	A1	19950202	WO 1994-US8119	19940718	<--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5534426	A	19960709	US 1993-94533	19930719	<--
	US 6514745	B1	20030204	US 1994-220602	19940325	
	AU 9473380	A1	19950220	AU 1994-73380	19940718	<--
	AU 700137	B2	19981224			
	EP 726908	A1	19960821	EP 1994-923544	19940718	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	JP 09507384	T2	19970729	JP 1995-505262	19940718	<--
	JP 2925740	B2	19990728			
	CA 2166981	C	20001107	CA 1994-2166981	19940718	

AB An isolated 46 kDa (by reducing SDS-PAGE) protein (**JNK**) with a serine/ threonine kinase activity that phosphorylates the c-Jun N-terminal activation domain and methods of detecting the protein are described.

CDNAs encoding the protein are also described. **JNK** phosphorylates c-Jun N-terminal activation domain which affects gene expression from AP-1 sites. Proteins binding c-jun were identified by affinity chromatog. against immobilized c-jun and a c-jun kinase activity was detected and characterized. The binding of the kinase to c-jun was strong with most of the complex stable to NaCl 2M. The roles of the protein in c-jun activation, its role in the interaction of c-jun and c-Ha-ras proteins and in T-cell activation are studied.

IT Immunoassay
(for **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Nucleic acid hybridization
(for detection of **JNK** protein kinase gene expression; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibiting **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Protein sequences
(of **JNK** protein kinase of human; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Acquired immune deficiency syndrome
(treatment of, inhibition of **JNK** protein kinase in; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(CD28, antibodies to, activation of **JNK** kinase by; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(CD3, antibodies to, activation of **JNK** kinase by; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Genetic element
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(RNA formation factor AP-1-responsive element, c-jun binding to, **JNK** protein kinase in; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Lymphocyte
(T-cell, c-jun function in activation of, **JNK** protein kinase in; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(colon, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Intestine, neoplasm
(colon, inhibitors, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Deoxyribonucleic acid sequences
(complementary, for **JNK** protein kinase of human; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Deoxyribonucleic acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(complementary, antisense, for inhibition of expression of **JNK** protein kinase gene; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Immunity
(disorder, treatment of, inhibition of **JNK** protein kinase in; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Ribonucleic acid formation factors
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(gene c-jun, fusion products with glutathione-S-transferase, in assays for **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Heart, disease
(**ischemia**, treatment of, inhibition of **JNK** protein kinase in; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(leukemia, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(lung non-small-cell carcinoma, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal, inhibiting **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Esophagus
(neoplasm, treatment of, inhibitors of **JNK** protein kinase for; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Prostate gland
(neoplasm, inhibitors, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Lung, neoplasm
(non-small-cell carcinoma, inhibitors, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(prostate gland, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(renal cell carcinoma, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Kidney, neoplasm
(renal cell carcinoma, inhibitors, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Arthritis
(rheumatoid, treatment of, inhibition of **JNK** protein kinase in; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(small intestine, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal

activation domain of c-jun protein)

IT Intestine, neoplasm
(small, inhibitors, inhibitors of **JNK** protein kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Blood vessel, disease
(vasculitis, treatment of, inhibition of **JNK** protein kinase in; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT 7440-70-2, Calcium, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(in activation of **JNK** kinase in T-lymphocytes; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT 16561-29-8, TPA
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synergism with A23187 in activation of **JNK** kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT 52665-69-7, Ionophore A23187
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synergism with TPA in activation of **JNK** kinase; serine/threonine protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

L6 ANSWER 102 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:513684 CAPLUS
DN 122:259844
TI A protein kinase that phosphorylates the N-terminal activation domain of the c-jun protein
IN Karin, Michael; Hibi, Masahiko; Lin, Anning
PA University of California, USA
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9503324	A1	19950202	WO 1994-US8120	19940718 <--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5534426	A	19960709	US 1993-94533	19930719 <--
	US 6514745	B1	20030204	US 1994-220602	19940325
	AU 9473668	A1	19950220	AU 1994-73668	19940718 <--
	AU 685484	B2	19980122		
	EP 728143	A1	19960828	EP 1994-922622	19940718 <--
	EP 728143	B1	20030305		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09500535	T2	19970121	JP 1995-505263	19940718 <--
	JP 2986548	B2	19991206		
	AT 233785	E	20030315	AT 1994-922622	19940718
PRAI	US 1993-94533	A	19930719		
	US 1994-220602	A	19940325		

PRAI WO 1994-US8120 W 19940718

PI WO 9503324 A1 **19950202**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9503324	A1	19950202	WO 1994-US8120	19940718 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5534426	A	19960709	US 1993-94533	19930719 <--
US 6514745	B1	20030204	US 1994-220602	19940325
AU 9473668	A1	19950220	AU 1994-73668	19940718 <--
AU 685484	B2	19980122		
EP 728143	A1	19960828	EP 1994-922622	19940718 <--
EP 728143	B1	20030305		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09500535	T2	19970121	JP 1995-505263	19940718 <--
JP 2986548	B2	19991206		
AT 233785	E	20030315	AT 1994-922622	19940718

AB An isolated protein (**JNK**) of 46kD (by reducing SDS-PAGE) with a serine and threonine kinase activity that phosphorylates the c-Jun N-terminal activation domain is described. The phosphorylation of the c-Jun N-terminal activation domain affects gene expression from AP-1 sites. The protein was identified as a kinase that bound very strongly to immobilized c-jun protein and the enzyme was found to phosphorylate Ser 63 and Ser 73 of c-jun. **JNK** binding was found to be essential for the Ha-ras and UV responsiveness of c-jun. Other factors affecting the activation of c-jun by **JNK** are described.

ST **JNK** protein kinase cjun activation; T lymphocyte activation **JNK** protein kinase

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(anti-idiotypic, to **JNK** protein kinase binding domain of c-jun; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Ultraviolet radiation
(c-jun activation by, **JNK** kinase in; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for **JNK** protein kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Nucleic acid hybridization
(for detection of **JNK** kinase gene expression; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Immunoassay
(for detection of **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Molecular association
(of c-jun protein and **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(to **JNK** protein kinase and c-jun domain binding the kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD28, antibodies to, activation of **JNK** kinase by; protein

kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD3, antibodies to, activation of **JNK** kinase by; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Genetic element
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(RNA formation factor AP-1-responsive element, c-jun interaction with, activation by **JNK** kinase in; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Lymphocyte
(T-cell, c-jun activation by **JNK** kinase in activation of; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(colon, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Intestine, neoplasm
(colon, inhibitors, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Ribonucleic acid formation factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene c-jun, **JNK** kinase activating; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Ribonucleic acid formation factors
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(gene c-jun, fusion products with glutathione-S-transferase, for detection of **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Heart, disease
(**ischemia**, treatment of, inhibition of c-jun activation in; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(leukemia, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(lung non-small-cell carcinoma, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Antibodies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(monoclonal, to **JNK** protein kinase and c-jun domain binding the kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Esophagus
(neoplasm, treatment of, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Prostate gland
(neoplasm, inhibitors, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Lung, neoplasm

(non-small-cell carcinoma, inhibitors, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p21c-Ha-ras, c-jun activation by, **JNK** kinase in; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(prostate gland, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(renal cell carcinoma, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Kidney, neoplasm
(renal cell carcinoma, inhibitors, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Neoplasm inhibitors
(small intestine, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT Intestine, neoplasm
(small, inhibitors, inhibitors of c-jun activation by **JNK** kinase; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT 162628-00-4
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence, **JNK** protein kinase-binding domain of c-jun protein; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT 50812-37-8D, Glutathione-S-transferase, fusion products with c-jun proteins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(antibodies to, activation of **JNK** kinase by; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT 7440-70-2, Calcium, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(in **JNK** kinase activation of c-jun by; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT 59865-13-3, Cyclosporin A
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of **JNK** kinase activation of c-jun by; protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

IT 155215-87-5, **JNK** protein kinase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(protein kinase that phosphorylates N-terminal activation domain of c-jun protein)

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     (FILE 'HOME' ENTERED AT 18:17:43 ON 21 JAN 2005)

     FILE 'CAPLUS, HCAPLUS' ENTERED AT 18:18:15 ON 21 JAN 2005
L1             0 S JNK (W) INHBIT?
L2             0 S JNK (P) INHBIT?
L3         12276 S JNK
L4          1278 S L3 AND (ATHEROSCLEROSIS OR RESTENOSIS OR ANGIOPLASTY OR HYPER
L5           639 DUP REM L4 (639 DUPLICATES REMOVED)
L6           102 S L5 AND PD<2000

=>
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(Uses)
(transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters)

IT 155215-87-5, Protein kinase **JNK**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transcriptional activation of scavenger receptor expression in human smooth muscle cells requires AP-1/c-Jun and NF-IL6; both AP-1 binding and **JNK** activation are induced by phorbol esters and oxidative stress)

L6 ANSWER 56 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:637314 CAPLUS
DN 130:23579
TI Differential activation of cardiac c-Jun amino-terminal kinase and extracellular signal-regulated kinase in angiotensin II-mediated hypertension.
AU Yano, Masahiko; Kim, Shokei; Izumi, Yasukatsu; Yamanaka, Shinya; Iwao, Hiroshi
CS Department of Pharmacology, Osaka City University Medical School, Shiga, Japan
SO Circulation Research (**1998**), 83(7), 752-760
CODEN: CIRUAL; ISSN: 0009-7330
PB Williams & Wilkins
DT Journal
LA English
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Circulation Research (**1998**), 83(7), 752-760
CODEN: CIRUAL; ISSN: 0009-7330
AB Two subgroups of mitogen-activated protein kinases, c-jun NH2-terminal kinase (**JNK**) and extracellular signal-regulated kinase (ERK), are thought to be involved in cultured cardiac myocyte **hypertrophy** and gene expression. To examine the in vivo activation of these kinases, the authors measured cardiac **JNK** and ERK activities in conscious rats subjected to acute or chronic angiotensin II (Ang II) infusion, by using in-gel kinase methods. About 50 mm Hg rise in blood pressure by Ang II (1000 ng · kg-1 · min-1) infusion caused larger activation of left ventricular **JNK** than ERK, via the AT1 receptor. In spite of short duration (about 30 min) of maximal blood pressure elevation by Ang II, **JNK** sustained the peak value (more than 5-fold increase) from 15 min up to at least 3 h. Similar activation of **JNK** was seen in the right ventricle. Thus, cardiac **JNK** activation by Ang II seems to be in part mediated by its direct action via the AT1 receptor. The dose-response relationships for Ang II-induced rises in blood pressure and cardiac **JNK** and ERK activation indicated that cardiac **JNK** or ERK was not activated by a mild increase in blood pressure and that cardiac **JNK** was activated by Ang II-mediated hypertension in a more sensitive manner than ERK. Cardiac **hypertrophy**, induced by chronic Ang II infusion, was preceded by **JNK** activation without ERK activation. Furthermore, gel mobility shift anal. showed that cardiac **JNK** activation was followed by increased activator protein-1 DNA binding activity due to c-Fos and c-Jun. These results provided the first evidence for the preferential activation of cardiac **JNK** in Ang II-induced hypertension and suggested that **JNK** might play some role in Ang II-induced cardiac hypertrophic response in vivo. However, further study is needed to elucidate the role of **JNK** in cardiac **hypertrophy** in vivo.
ST cJun kinase angiotensin II hypertension cardiac **hypertrophy**

IT Heart, disease
(**hypertrophy**; cardiac c-Jun amino-terminal kinase and extracellular signal-regulated kinase activation in angiotensin II-mediated hypertension)

L6 ANSWER 57 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:589366 CAPLUS
DN 129:272307
TI Crystal structure of JNK3: a kinase implicated in neuronal apoptosis
AU Xie, Xiaoling; Gu, Yong; Fox, Ted; Coll, Joyce T.; Fleming, Mark A.; Markland, William; Caron, Paul R.; Wilson, Keith P.; Su, Michael S-S.
CS Vertex Pharmaceuticals Incorporated, Cambridge, MA, 02139-4211, USA
SO Structure (London) (**1998**), 6(8), 983-991
CODEN: STRUE6; ISSN: 0969-2126
PB Current Biology Ltd.
DT Journal
LA English
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Structure (London) (**1998**), 6(8), 983-991
CODEN: STRUE6; ISSN: 0969-2126
AB The c-Jun N-terminal kinases (JNKs) are members of the mitogen-activated protein (MAP) kinase family, and regulate signal transduction in response to environmental stress. Activation and nuclear localization of JNK3, a neuronal-specific isoform of **JNK**, has been associated with hypoxic and **ischemic** damage of CA1 neurons in the hippocampus. Knockout mice lacking JNK3 showed reduced apoptosis of hippocampal neurons and reduced seizure induced by kainic acid, a glutamate-receptor agonist. Thus, JNK3 may be important in the pathol. of neurol. disorders and is of significant medical interest. Here, the authors report the structure of unphosphorylated JNK3 in complex with adenylyl imidodiphosphate (AMP-PNP), an ATP analog. JNK3 was found to have a typical kinase fold, with the ATP-binding site situated within a cleft between the N- and C-terminal domains. In contrast to other known MAP kinase structures, the ATP-binding site of JNK3 was well-ordered; the glycine-rich nucleotide-binding sequence formed a β-strand-turn-β-strand structure over the nucleotide. Unphosphorylated JNK3 assumed an open conformation, in which the N- and C-terminal domains were twisted apart relative to their positions in cAMP-dependent protein kinase. The rotation was found to lead to the misalignment of some of the catalytic residues. The phosphorylation lip of JNK3 partially blocked the substrate-binding site. This is the 1st **JNK** structure to be determined, providing a unique opportunity to compare structures from the 3 MAP kinase subfamilies. The structure revealed atomic-level details of the shape of JNK3 and the interactions between the kinase and the nucleotide. The misalignment of catalytic residues and occlusion of the active site by the phosphorylation lip may account for the low activity of unphosphorylated JNK3. The structure provides a framework for understanding the substrate specificity of different **JNK** isoforms, and should aid the design of selective JNK3 inhibitors.
IT 69977-25-9D, complexes with **JNK** kinase 155215-87-5D, **JNK** kinase, isoform 3, complexes with Mg-AMP-PNP
RL: PRP (Properties)
(crystal structure of JNK3 kinase complexed with Mg-AMP-PNP)

L6 ANSWER 58 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:582652 CAPLUS
DN 129:286311
TI Prostaglandin F2α (PGF2α) and the isoprostane, 8,12-iso-isoprostane F2α-III, induce cardiomyocyte **hypertrophy**. Differential activation of downstream signaling pathways

AU Kunapuli, Priya; Lawson, John A.; Rokach, Joshua A.; Meinkoth, Judy L.; FitzGerald, Garret A.

CS Center for Experimental Therapeutics, University of Pennsylvania, Philadelphia, PA, 19104, USA

SO Journal of Biological Chemistry (**1998**), 273(35), 22442-22452
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Prostaglandin F2α (PGF2α) and the isoprostane, 8,12-iso-isoprostane F2α-III, induce cardiomyocyte **hypertrophy**. Differential activation of downstream signaling pathways

SO Journal of Biological Chemistry (**1998**), 273(35), 22442-22452
CODEN: JBCHA3; ISSN: 0021-9258

AB Prostaglandin receptors may be activated by their cognate ligand or by free radical catalyzed isoprostanes, products of arachidonic acid peroxidn. For example, PGF2α causes **hypertrophy** of neonatal rat ventricular myocytes, via the PGF2α receptor (FP). However, the FP may also be activated by the isoprostane, 8,12-iso-isoprostane F2α-III (iPF2α-III). Both ligands induce myocyte **hypertrophy** with overlapping potencies. Interestingly, the hypertrophic effects of these two agonists on cardiomyocytes are additive. Furthermore, the preference of these two agonists for activation of intracellular signal transduction pathways differs in several respects. Thus, PGF2α and iPF2α-III stimulate inositol phosphate formation with EC50 values of 50 nM and 3.5 μM, resp. Moreover, PGF2α causes a robust activation (.apprx.50-fold) of Erk2, whereas iPF2α-III has no effect. Similarly, PGF2α causes translocation of cytosolic phospholipase A2 and also results in a 7-fold increment in the formation of 6-keto-PGF1α, whereas 8,12-iso-iPF2α-III exerts no effect on this pathway. Both agonists are equally potent in activating JNK1 and c-Jun, whereas neither activates the p38 kinase. Both PGF2α and iPF2α-III activate the p70S6 kinase (p70S6K), but not Akt, downstream of phosphatidylinositol-3-kinase (PI3K). However, both wortmannin, a PI3K inhibitor, and rapamycin, an inhibitor of p70S6K activity, inhibit iPF2α-III -induced myocyte **hypertrophy**, with IC50 values of 60 and 3 nM, resp., whereas neither compound abrogates the PGF2α-mediated response. Thus, both PGF2α and iPF2α-III induce myocyte **hypertrophy** via discrete signaling pathways. Although both agonists signal via the **JNK** pathway to initiate changes in c-Jun-dependent gene transcription, PGF2α preferentially activates the MEK-Erk2-cytosolic phospholipase A2 pathway. In contrast, the PI3K-p70S6K pathway appears to be essential for iPF2α-III-induced myocyte **hypertrophy**.

ST PGF2 isoprostane F2 heart **hypertrophy**; signal transduction cardiomyocyte PGF2 isoprostane F2

IT Signal transduction, biological
(PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation of downstream signaling pathways)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-jun; PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation of downstream signaling pathways)

IT Heart, disease
(**hypertrophy**; PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation

of downstream signaling pathways)
IT Biological transport
(intracellular; PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation of downstream signaling pathways)
IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pp70s6k; PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation of downstream signaling pathways)
IT Heart
(ventricle, myocyte; PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation of downstream signaling pathways)
IT 551-11-1, Prostaglandin F2α 197151-16-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation of downstream signaling pathways)
IT 58962-34-8 68247-19-8, Inositol phosphate 115926-52-8, Phosphatidylinositol-3 kinase 137632-08-7, Erk2 kinase 155215-87-5, c-Jun-N-terminal kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation of downstream signaling pathways)
IT 9001-84-7, Phospholipase A2 142805-58-1, Mitogen-activated protein kinase kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PGF2α and iso-isoprostane F2α-III induce cardiomyocyte **hypertrophy** by differential activation of downstream signaling pathways)

L6 ANSWER 59 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:560599 CAPLUS
DN 129:273404
TI "Stress-responsive" mitogen-activated protein kinases (c-Jun N-terminal kinases and p38 mitogen-activated protein kinases) in the myocardium
AU Sugden, Peter H.; Clerk, Angela
CS NHLI Division, Imperial College School of Medicine, London, SW3 6LY, UK
SO Circulation Research (**1998**), 83(4), 345-352
CODEN: CIRUAL; ISSN: 0009-7330
PB Williams & Wilkins
DT Journal; General Review
LA English
RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Circulation Research (**1998**), 83(4), 345-352
CODEN: CIRUAL; ISSN: 0009-7330
AB A review with 79 refs. on the regulation of **JNK** and p38-MAPK cascades in the myocardium and activation the mitogen-activated protein kinases by cellular stresses and G-protein-coupled receptor agonists.
ST review **JNK** p38 MAPK stress heart
IT Heart, disease
(**hypertrophy**; stress-responsive mitogen-activated protein kinases (c-Jun N-terminal kinases and p38 mitogen-activated protein kinases) in myocardium)

L6 ANSWER 60 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:550434 CAPLUS
DN 129:185782
TI Daxx, a novel fas-binding protein that activates **jnk** and apoptosis
IN Yang, Xiaolu; Khosravi-Far, Roya; Chang, Howard Y.; Baltimore, David
PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834946	A1	19980813	WO 1998-US2588	19980212 <--
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6159731	A	20001212	US 1998-22983	19980212
PRAI	US 1997-37919P	P	19970212		
	US 1997-51753P	P	19970626		

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Daxx, a novel fas-binding protein that activates **jnk** and apoptosis
PI WO 9834946 A1 **19980813**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834946	A1	19980813	WO 1998-US2588	19980212 <--
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6159731	A	20001212	US 1998-22983	19980212

AB Nucleic acids encoding the Daxx protein, including fragments and biol. functional variants are described. Also included are polypeptides and fragments thereof encoded by such nucleic acids, and antibodies relating thereto. Methods and products for using such nucleic acids and polypeptides also are provided. Daxx was shown to activate the **JNK**/SAPK pathway and defective Daxx signaling was shown in autoimmune lymphoproliferative disorder (ALPS).

ST Fas binding protein **JNK** apoptosis activation; sequence mouse human Fas binding protein; autoimmune lymphoproliferative disorder **JNK** activation ASK1

IT Signal transduction, biological
(Daxx and FADD activate apoptosis downstream of Fas by distinct cooperative pathways; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(FADD; Daxx and FADD activate apoptosis downstream of Fas by distinct cooperative pathways; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT Protein motifs
(Fas death domain; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT Lymphoma
(NK; method to treat abnormal Fas-mediated apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT **Transplant** rejection
(allotransplant, method to treat abnormal Fas-mediated apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT Antisense DNA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(antisense inhibiting gene expression; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Apoptosis
Drug delivery systems
Genetic vectors
Protein sequences
cDNA sequences
(daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Fas antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Lymphoproliferative disorders
(defective Daxx signaling in autoimmune lymphoproliferative disorders; treatment of insufficient apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Gene
(expression, antisense inhibiting gene expression; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fas-binding protein Daxx; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Immunoglobulins
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fragments, Fab or F(ab)2 or CDR3 region fragment; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Hepatitis
(fulminant, method to treat abnormal Fas-mediated apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT **Transplant** and Transplantation
(graft-vs.-host reaction, method to treat abnormal Fas-mediated apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Liver, disease
Liver, disease
(hyperplasia, method to treatment of insufficient apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Leukemia
(large granular lymphocytic, method to treat abnormal Fas-mediated apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)
IT Hyperplasia
Hyperplasia
(liver, method to treatment of insufficient apoptosis associated with;

daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT Animal cell
(mammalian, method for increasing or decreasing **JNK** signal transduction in mammalian cells; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT T cell (lymphocyte)
(method to treat abnormal Fas-mediated apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT Autoimmune disease
(method to treatment of insufficient apoptosis associated with; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT 155215-87-5
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT 211485-61-9 211623-45-9, 629-740-Protein Daxx (human Fas-binding)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence of dominant-neg. Daxx variant decreasing **JNK** signal transduction; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT 209064-31-3, Protein (human clone B2046 gene DAXX)
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT 185464-61-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(apoptosis signal-regulating kinase 1 ASK1 is downstream target of Daxx; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT 193636-95-2, Protein Daxx (mouse thymus gland) 193737-04-1, GenBank AF006040
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

IT 211507-27-6 211623-43-7 211623-44-8
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; daxx novel fas-binding protein that activates **jnk** and apoptosis from mouse and human)

L6 ANSWER 61 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:541433 CAPLUS
DN 129:258771
TI Stimulation of multiple mitogen-activated protein kinase sub-families by oxidative stress and phosphorylation of the small heat shock protein, HSP25/27, in neonatal ventricular myocytes
AU Clerk, Angela; Michael, Ashour; Sugden, Peter H.
CS NHLI Division (Cardiac Medicine), Imperial College School of Medicine, London, SW3 6LY, UK
SO Biochemical Journal (**1998**), 333(3), 581-589
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal

LA English
RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Biochemical Journal (**1998**), 333(3), 581-589
CODEN: BIJOAK; ISSN: 0264-6021
IT Heart, disease
(**hypertrophy**; stimulation of multiple mitogen-activated protein kinase sub-families by oxidative stress and phosphorylation of small heat shock protein, HSP25/27, in neonatal ventricular myocytes in relation to)
IT 137632-07-6, Kinase (phosphorylating), protein, ERK1 137632-08-7, Kinase (phosphorylating), protein, ERK2 142243-02-5, Kinase (phosphorylating), mitogen-activated protein 146838-31-5, p54SAPK Kinase 155215-87-5, **JNK**-46 protein kinase 165245-96-5, p38 MAP kinase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(stimulation of multiple mitogen-activated protein kinase sub-families by oxidative stress and phosphorylation of small heat shock protein, HSP25/27, in neonatal ventricular myocytes)

L6 ANSWER 62 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:515635 CAPLUS
DN 129:225687
TI Epigallocatechin suppression of proliferation of vascular smooth muscle cells: correlation with c-jun and **JNK**
AU Lu, Liang-Huei; Lee, Shoei-Sheng; Huang, Huei-Chen
CS Department of Pharmacology, National Taiwan University, Taipei, Taiwan
SO British Journal of Pharmacology (**1998**), 124(6), 1227-1237
CODEN: BJPCBM; ISSN: 0007-1188
PB Stockton Press
DT Journal
LA English
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Epigallocatechin suppression of proliferation of vascular smooth muscle cells: correlation with c-jun and **JNK**
SO British Journal of Pharmacology (**1998**), 124(6), 1227-1237
CODEN: BJPCBM; ISSN: 0007-1188
AB The mechanisms of the antiproliferative effect of epigallocatechin, one of the catechin derivs. found in green tea, in vascular smooth muscle cells were studied. The proliferative response was determined from the uptake of tritiated thymidine. In the concentration range of 10-6 to 10-4 M, catechin, epicatechin, epigallocatechin, epicatechin gallate and epigallocatechin gallate concentration-dependently inhibited the proliferative response stimulated
by serum in rabbit cultured vascular smooth muscle cells. Catechin and epicatechin were less effective in inhibiting the serum-stimulated smooth muscle cell proliferation, indicating that the galloyl group may be important for full inhibitory activity. Epigallocatechin (EGC) inhibited the proliferative responses in different cells including rat aortic smooth muscle cells (A7r5 cells), rabbit cultured aortic smooth muscle cells, human coronary artery smooth muscle cells, and human CEM lymphocytes in a concentration-dependent manner. The possible mechanisms of the antiproliferative
effect of EGC were further studied in A7r5 cells. The membranous protein tyrosine kinase activity stimulated by serum in A7r5 cells was significantly reduced by 10-5 M EGC. In contrast, the cytosolic protein kinase C activity stimulated by phorbol ester was unaffected by directly incubating with EGC (10-6-10-4 M). The authors also performed Western blot anal. using the anti-phosphotyrosine monoclonal antibody PY-20. EGC (10-5 M) reduced the levels of tyrosine phosphorylated proteins with

different mol. wts., indicating that EGC may inhibit the protein tyrosine kinase activity or stimulate the protein phosphatase activity. Reverse transcription-polymerase chain reaction anal. of c-fos, c-jun and c-myc mRNA levels demonstrated that c-jun mRNA level after serum-stimulation was significantly reduced by 10-5 M EGC. However, the reduction of c-fos and c-myc mRNA levels by 10-5 M EGC did not achieve significance. Western blot anal. using the antibody against **JNK** (c-jun N-terminal kinase) and ERK (extracellular signal-regulated kinase) demonstrated that the level of phosphorylated JNK1, but not phosphorylated ERK1 and ERK2, was reduced by 10-5 M EGC. Direct measurement of kinase activity by immune complex kinase assay confirmed that JNK1 activity was inhibited by EGC treatment. These results demonstrate that EGC preferentially reduced the activation of **JNK**/SAPK (stress-activated protein kinase) signal transduction pathway. It is suggested that the antiproliferative effect of epigallocatechin on vascular smooth muscle cells may partly be mediated through inhibition of protein tyrosine kinase activity, reducing c-jun mRNA expression and inhibiting JNK1 activation. Tea catechins may be useful as a template for the development of drugs to prevent the pathol. changes of **atherosclerosis** and post-**angioplasty restenosis**.

IT Structure-activity relationship
(antiproliferative; epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-fos; epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-jun; epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-myc; epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

IT Cytotoxic agents
(epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

IT Proliferation inhibition
(proliferation inhibitors; epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

IT Blood vessel
(smooth muscle; epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

IT 154-23-4, (+)-Catechin 490-46-0, (-)-Epicatechin 970-74-1, (-)-Epigallocatechin 989-51-5 1257-08-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

IT 80449-02-1, Kinase (phosphorylating), protein (tyrosine) 137632-07-6, ERK1 kinase 137632-08-7, ERK2 kinase 141436-78-4, Protein kinase C 155215-87-5, JNK1 kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(epigallocatechin and its derivs. suppression of proliferation of vascular smooth muscle cells and correlation with c-jun and **JNK** and structure)

L6 ANSWER 63 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:452829 CAPLUS
DN 129:160182
TI Lasting N-terminal phosphorylation of c-Jun and activation of c-Jun N-terminal kinases after neuronal injury
AU Herdegen, Thomas; Claret, Francois-Xavier; Kallunki, Tuula; Martin-Villalba, Ana; Winter, Christine; Hunter, Tony; Karin, Michael
CS Laboratory of Gene Regulation and Signal Transduction, Department of Pharmacology, University of California, La Jolla, CA, 92093-0636, USA
SO Journal of Neuroscience (**1998**), 18(14), 5124-5135
CODEN: JNRSDS; ISSN: 0270-6474
PB Society for Neuroscience
DT Journal
LA English
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Neuroscience (**1998**), 18(14), 5124-5135
CODEN: JNRSDS; ISSN: 0270-6474
AB Transcription factor c-Jun is proposed to control neuronal cell death and survival, but its activation by N-terminal phosphorylation and the underlying activity of the c-Jun N-terminal kinases (JNKs) remain to be elucidated in the adult mammalian brain. The authors generated a polyclonal antiserum that specifically recognizes c-Jun phosphorylated at its serine 73 (S73) residue after UV irradiation of 3T3 cells. Disruption of the c-jun locus in 3T3 cells abolished this reaction, and retransfection of the human c-jun at the c-jun-/- background restored it. The phospho-c-Jun antiserum was used to visualize N-terminally phosphorylated c-Jun in the adult rat brain with cellular resolution Prolonged c-Jun S73 phosphorylation was detected in affected neurons up to 5 d after transient occlusion of medial cerebral artery or up to 50 d after transection of central nerve fiber tracts. After cerebral **ischemia** -reperfusion, phosphorylation of c-Jun was linked with induced expression of Fas-ligand (APO-1, CD95-ligand), whose gene is a putative c-Jun/AP-1 target, and with terminal deoxynucleotidyl transferase-mediated biotinylated UTP nick end labeling (TUNEL) reactivity, a marker for apoptosis. After nerve fiber transection, however, lasting c-Jun phosphorylation occurred in axotomized neurons neg. for Fas-ligand or TUNEL and regardless of degeneration or survival. In contrast to these lasting phosphorylation patterns, transient seizure activity by pentylenetetrazole provoked only a brief c-Jun phosphorylation and **JNK** activation. In exts. from **ischemic** or axotomized brain compartments, c-Jun phosphorylation correlated with enhanced long-term **JNK** activity, and in-gel kinase assays visualized proteins with sizes corresponding to **JNK** isoforms as the only c-Jun N-terminally phosphorylating enzymes. These results demonstrate that lasting c-Jun S73 phosphorylation and **JNK** activity are part of neuronal stress response after neurodegenerative disorders in the adult mammalian brain with Fas-ligand as a putative apoptotic effector.
IT Brain, disease
(**ischemia**, transient; lasting N-terminal phosphorylation of c-Jun and activation of c-Jun N-terminal kinases after neuronal injury)

L6 ANSWER 64 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:379955 CAPLUS
DN 129:120971
TI Activation of mitogen-activated protein kinases and activator protein-1 in myocardial **infarction** in rats
AU Shimizu, Naruhito; Yoshiyama, Minoru; Omura, Takashi; Hanatani, Akihisa; Kim, Shokei; Takeuchi, Kazuhide; Iwao, Hiroshi; Yoshikawa, Junichi
CS First Dep. Internal Med., Osaka City Univ. Med. School, Osaka, 545-0051, Japan
SO Cardiovascular Research (**1998**), 38(1), 116-124
CODEN: CVREAU; ISSN: 0008-6363
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Activation of mitogen-activated protein kinases and activator protein-1 in myocardial **infarction** in rats
SO Cardiovascular Research (**1998**), 38(1), 116-124
CODEN: CVREAU; ISSN: 0008-6363
AB The purpose of this study was to examine the activation of mitogen-activated protein kinases (MAPK) plus activator protein-1 (AP-1) and nuclear factor-κB (NF-κB) DNA binding activities, all of which seem to be important in a signal transduction cascade upstream of the increased level of mRNA expression observed after myocardial **infarction**. Myocardial **infarction** was produced in Wistar rats. The activities of MAPKs in the **ischemic** region were measured using an in-gel kinase method or an in vitro kinase method. AP-1 and NF-κB binding was determined using an electrophoretic mobility shift assay. Levels of transforming growth factor β1(TGF-β1) and collagen I and III mRNAs were analyzed by Northern blot hybridization. P42 Extracellular signal-regulated kinase (ERK), p44ERK and p38MAPK activities increased 5.2-fold, 4.3-fold and 1.9-fold, resp., at 5 min after coronary artery ligation but returned to normal levels by 30 min. P55 c-Jun NH2-terminal kinase (**JNK**) and p46JNK activities increased 4.0-fold and 3.2-fold, resp., at 15 min and returned to normal levels by 24 h after ligation. AP-1 DNA and NF-κB binding activities increased 8.7-fold and 7.1-fold, resp., at 3 days but returned to normal levels by 7 days after ligation. Interestingly, analyses of the levels of TGF-β1, collagen I and III mRNAs revealed increases of 6.3-fold, 15.2-fold and 12.0-fold, resp., at 1 wk after myocardial **infarction**. Myocardial **ischemia** increased MAPK activities, which were followed by enhancement of AP-1 and NF-κB DNA binding activity in areas of myocardial **infarction** in rats. These signal transduction mechanisms may contribute to the myocardial **ischemia** and injury associated with myocardial **infarction** by causing an increased expression of TGF-β1 mRNA, collagen I and III in the area.
ST myocardial **infarction** MAP kinase AP1 NFkappaB
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1); activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats)
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-κB (nuclear factor κB); activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats)
IT mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM

(Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(TGF-β1 and collagens I and III; activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats in relation to)

IT Signal transduction, biological
Transcription, genetic
(activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats in relation to)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats in relation to)

IT Gene
(expression; activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats in relation to)

IT Heart, disease
(**infarction**; activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats)

IT Heart, disease
(**ischemia**; activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats in relation to)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type I, α1(I)-chain, mRNA; activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats in relation to)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type III, α1(III)-chain, mRNA; activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats in relation to)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β1-, mRNA; activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats in relation to)

IT 155215-87-5, **JNK**-46 protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**JNK**-46 and **JNK**-55; activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats)

IT 137632-07-6, P44 ERK-1 kinase 137632-08-7, p42 ERK-2 kinase
142243-02-5, Kinase (phosphorylating), mitogen-activated protein
165245-96-5, Protein kinase p38mapk
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of mitogen-activated protein kinases, activator protein-1, and NF-κB in myocardial **infarction** in rats)

L6 ANSWER 65 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:355795 CAPLUS
DN 129:93800

TI Activation of **JNK** in the remote myocardium after large myocardial **infarction** in rats
AU Li, Wei Gen; Zaheer, Asgar; Coppey, Lawrence; Oskarsson, Helgi J.
CS Departments of Internal Medicine and Neurology, University of Iowa, Iowa City, IA, 52242, USA
SO Biochemical and Biophysical Research Communications (**1998**), 246(3), 816-820
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Activation of **JNK** in the remote myocardium after large myocardial **infarction** in rats
SO Biochemical and Biophysical Research Communications (**1998**), 246(3), 816-820
CODEN: BBRCA9; ISSN: 0006-291X
AB A large myocardial **infarction** (MI) causes a chronic hemodynamic load on the uninjured remote myocardium (RM). This may lead to oxidative stress, activation of stress-induced cell signaling and increase in myocyte apoptosis. MI was produced in 6 rats (INF) while 4 rats underwent sham operation (CON). At four weeks, there was 128% increase in right ventricular **hypertrophy** in the hearts from INF vs. CON. Western blot anal. showed 3.8 fold increase in **JNK** phosphorylation within the RM from INF vs. CON, confirmed by a 4.2 fold increase in **JNK** kinase activity. There was a 52% increase in TBARS within the RM from INF vs. CON, suggesting increased lipid peroxidn. Furthermore, there was a twofold increase in myocyte apoptosis within the RM in INF vs. CON. We conclude that the RM from INF is associated with activation of **JNK**, increased oxidative stress and enhanced myocyte apoptosis.
ST myocardial **infarction** heart **JNK** kinase
IT Apoptosis
Oxidative stress, biological
(activation of **JNK** in remote myocardium after large myocardial **infarction** in rats)
IT Heart, disease
(**infarction**; activation of **JNK** in remote myocardium after large myocardial **infarction** in rats)
IT Peroxidation
(lipid; activation of **JNK** in remote myocardium after large myocardial **infarction** in rats)
IT Lipids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(peroxidn.; activation of **JNK** in remote myocardium after large myocardial **infarction** in rats)
IT Phosphorylation, biological
(protein; activation of **JNK** in remote myocardium after large myocardial **infarction** in rats)
IT Heart, disease
(ventricle, **hypertrophy**; activation of **JNK** in remote myocardium after large myocardial **infarction** in rats)
IT 155215-87-5, **JNK** kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of **JNK** in remote myocardium after large myocardial **infarction** in rats)

L6 ANSWER 66 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:350820 CAPLUS

DN 129:80035
TI Opposing effects of Jun kinase and p38 mitogen-activated protein kinases on cardiomyocyte **hypertrophy**
AU Nemoto, Shino; Sheng, Zelin; Lin, Anning
CS Department of Pathology, Division of Molecular and Cellular Pathology, University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SO Molecular and Cellular Biology (**1998**), 18(6), 3518-3526
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
RE.CNT 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Opposing effects of Jun kinase and p38 mitogen-activated protein kinases on cardiomyocyte **hypertrophy**
SO Molecular and Cellular Biology (**1998**), 18(6), 3518-3526
CODEN: MCEBD4; ISSN: 0270-7306
AB C-Jun N-terminal protein kinase (**JNK**) and p38, two distinct members of the mitogen-activated protein (MAP) kinase family, regulate gene expression in response to various extracellular stimuli, yet their physiol. functions are not completely understood. In this report we show that **JNK** and p38 exerted opposing effects on the development of myocyte **hypertrophy**, which is an adaptive physiol. process characterized by expression of embryonic genes and unique morphol. changes. In rat neonatal ventricular myocytes, both **JNK** and p38 were stimulated by hypertrophic agonists like endothelin-1, phenylephrine, and leukemia inhibitory factor. Expression of MAP kinase kinase 6b (EE), a constitutive activator of p38, stimulated the expression of atrial natriuretic factor (ANF), which is a genetic marker of in vivo cardiac **hypertrophy**. Activation of p38 was required for ANF expression induced by the hypertrophic agonists. Furthermore, a specific p38 inhibitor, SB202190, significantly changed hypertrophic morphol. induced by the agonists. Surprisingly, activation of **JNK** led to inhibition of ANF expression induced by MEK kinase 1 (MEKK1) and the hypertrophic agonists. MEKK1-induced ANF expression was also neg. regulated by expression of c-Jun. Our results demonstrate that p38 mediates, but **JNK** suppresses, the development of myocyte **hypertrophy**.
ST p38 MAP Jun kinase heart **hypertrophy**
IT Heart, disease
(**hypertrophy**; opposing effects of Jun kinase and p38 mitogen-activated protein kinase on cardiomyocyte **hypertrophy**)
IT Heart
(myocyte; opposing effects of Jun kinase and p38 mitogen-activated protein kinase on cardiomyocyte **hypertrophy**)
IT Leukemia inhibitory factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opposing effects of Jun kinase and p38 mitogen-activated protein kinase on cardiomyocyte **hypertrophy**)
IT 155215-87-5 165245-96-5, p38 Mitogen-activated protein kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(opposing effects of Jun kinase and p38 mitogen-activated protein kinase on cardiomyocyte **hypertrophy**)
IT 123626-67-5, Endothelin-1 146702-84-3, MEK kinase 1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opposing effects of Jun kinase and p38 mitogen-activated protein kinase on cardiomyocyte **hypertrophy**)

IT 85637-73-6, Atriopeptin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(opposing effects of Jun kinase and p38 mitogen-activated protein kinase on cardiomyocyte **hypertrophy**)

L6 ANSWER 67 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:340832 CAPLUS
DN 129:121000
TI Angiotensin blockade inhibits activation of mitogen-activated protein kinases in rat balloon-injured artery
AU Kim, Shokei; Izumi, Yasukatsu; Yano, Masahiko; Hamaguchi, Akinori; Miura, Katsuyuki; Yamanaka, Shinya; Miyazaki, Hitoshi; Iwao, Hiroshi
CS Department of Pharmacology, Osaka City University Medical School, Osaka, 545, Japan
SO Circulation (**1998**), 97(17), 1731-1737
CODEN: CIRCAZ; ISSN: 0009-7322
PB Williams & Wilkins
DT Journal
LA English
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Circulation (**1998**), 97(17), 1731-1737
CODEN: CIRCAZ; ISSN: 0009-7322
AB The effect of balloon injury on the arterial signal transduction pathway has not been examined In vitro studies show that extracellular signal-regulated kinases (ERKs) and c-Jun NH2-terminal kinases (JNKs), belonging to the mitogen-activated protein kinase (MAPK) family, play a critical role in the activation of transcription factor activator protein-1 (AP-1) and cell proliferation or apoptosis. However, the activation and role of MAPKs in vascular diseases in vivo remain to be determined Therefore, we examined the effect of balloon injury on arterial MAPKs and the possible role of angiotensin II. Arterial **JNK** and ERK activities were measured by in-gel kinase assay, AP-1 DNA binding activity was determined by gel mobility shift anal. After balloon injury of rat carotid artery, **JNK** (p46JNK and p55JNK) and ERK (p44ERK and p42ERK) activities were increased as early as 2 min, reached their peak (6- to 18-fold) at 5 min, and thereafter rapidly declined to control levels. **JNK** and ERK activations were followed by a 3.9-fold increase in arterial AP-1 DNA binding activity, which contained c-Jun and c-Fos proteins. Arterial **JNK** activation at 2 or 5 min was remarkably suppressed by E4177 (an angiotensin AT1 receptor antagonist) and cilazapril (an ACE inhibitor). E4177 also prevented activation of ERKs by suppressing their tyrosine phosphorylation, whereas cilazapril failed to prevent such activation. The increased AP-1 DNA binding activity was significantly inhibited by both E4177 and cilazapril. Arterial JNKs and ERKs are dramatically dramatically activated by balloon injury associated with the activation of the AP-1 complex. These MAPK activations, followed by AP-1 activation, are mediated at least in part by the AT1 receptor. Thus, activation of JNKs and ERKs may be responsible for balloon injury-induced neointima formation.
ST balloon injury arterial signal transduction MAPK; mitogen activated protein kinase balloon injury; angiotensin II **JNK** ERK vascular neointima; p46JNK p55JNK AP1 AT1 receptor artery; p44ERK p42ERK AP1 AT1 receptor artery; ACE inhibitor balloon injury MAPK signaling; **angioplasty** injury MAPK AP1 AT1 receptor
IT Artery
(**angioplasty**, injury; angiotensin blockade inhibiting activation of mitogen-activated protein kinases in rat balloon-injured artery)

L6 ANSWER 68 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:330411 CAPLUS
DN 129:66326
TI Cardiac **hypertrophy** induced by mitogen-activated protein kinase kinase 7, a specific activator for c-Jun NH2-terminal kinase in ventricular muscle cells. [Erratum to document cited in CA128:293479]
AU Wang, Yibin; Su, Bing; Sah, Valerie P.; Brown, Joan Heller; Han, Jiahuai; Chien, Kenneth R.
CS Department of Medicine, University of California at San Diego, La Jolla, CA, 92093, USA
SO Journal of Biological Chemistry (**1998**), 273(20), 12684
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
TI Cardiac **hypertrophy** induced by mitogen-activated protein kinase kinase 7, a specific activator for c-Jun NH2-terminal kinase in ventricular muscle cells. [Erratum to document cited in CA128:293479]
SO Journal of Biological Chemistry (**1998**), 273(20), 12684
CODEN: JBCHA3; ISSN: 0021-9258
ST erratum heart reperfusion injury **hypertrophy JNK**; heart reperfusion injury **hypertrophy JNK** erratum; reperfusion injury **hypertrophy JNK** p38 erratum
IT Heart, disease
(**hypertrophy**; **JNK** and p38 roles in cardiac **hypertrophy** (Erratum))
IT Reperfusion
(injury; **JNK** and p38 roles in cardiac **hypertrophy** (Erratum))
IT Heart, disease
(**ischemia**; **JNK** and p38 roles in cardiac **hypertrophy** (Erratum))
IT Heart
(myocyte; **JNK** and p38 roles in cardiac **hypertrophy** (Erratum))
IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(p38; **JNK** and p38 roles in cardiac **hypertrophy** (Erratum))
IT Heart
(ventricle; **JNK** and p38 roles in cardiac **hypertrophy** (Erratum))
IT 155215-87-5 172308-13-3 192230-91-4, MAP kinase kinase 7 194739-73-6
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**JNK** and p38 roles in cardiac **hypertrophy** (Erratum))
IT 85637-73-6, Atrial natriuretic factor
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**JNK** and p38 roles in cardiac **hypertrophy** (Erratum))

L6 ANSWER 69 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:323142 CAPLUS
DN 129:592
TI Therapeutic methods for vascular injury using inhibition of the Ras signal transduction pathway
IN Chien, Shu; Shyy, John Y.-J.
PA Regents of the University of California, San Diego, USA; Shyy, John Y. J.

SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9819686	A1	19980514	WO 1997-US20404	19971107 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6335010	B1	20020101	US 1997-884866	19970630
	AU 9851739	A1	19980529	AU 1998-51739	19971107 <--
PRAI	US 1996-30358P	P	19961108		
	US 1997-884866	A2	19970630		
	WO 1997-US20404	W	19971107		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI WO 9819686 A1 **19980514**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9819686	A1	19980514	WO 1997-US20404	19971107 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6335010	B1	20020101	US 1997-884866	19970630
	AU 9851739	A1	19980529	AU 1998-51739	19971107 <--

AB Methods are provided for treating disorders associated with vascular injury from mech. stimuli, including **restenosis**, **atherosclerosis** and reperfusion injury. In one embodiment of the invention gene therapy techniques are applied using genes encoding a variety of proteins that play key roles in transducing an extracellular signal through to the nucleus, including src, Ras, MEKK and **JNK**. These proteins are mutated such that they are rendered signal transduction incompetent, thus abrogating their ability to induce a cellular response. The invention further encompasses viral gene therapy vectors containing genes encoding these signaling incompetent mutants and pharmaceutical compns. Addnl. embodiments of the invention encompass alternative means of inhibiting the key signal transduction pathways related to mech. injury. One alternative includes the use of antisense versions of genes encoding key proteins such as src, Ras, MEKK, **JNK** and the like. Chemical compds. acting as enzymic inhibitors or disrupters of protein-protein interactions are also contemplated by the invention.

ST Ras signal transduction inhibition vascular therapeutic; gene therapy vascular injury Ras pathway; **restenosis** Ras signal transduction inhibition; **atherosclerosis** Ras signal transduction inhibition; reperfusion injury Ras signal transduction inhibition

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HA-**JNK**; therapeutic methods for vascular injury using inhibition of Ras signal transduction pathway)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**JNK**(K-R); therapeutic methods for vascular injury using inhibition of Ras signal transduction pathway)
IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**Jnk**; therapeutic methods for vascular injury using inhibition of Ras signal transduction pathway)
IT Artery
(**angioplasty**; therapeutic methods for vascular injury using inhibition of Ras signal transduction pathway)
IT Artery, disease
(**restenosis**; therapeutic methods for vascular injury using inhibition of Ras signal transduction pathway)
IT 142243-02-5 155215-87-5, **Jnk** kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic methods for vascular injury using inhibition of Ras signal transduction pathway)

L6 ANSWER 70 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:309196 CAPLUS
DN 129:80066
TI DNA binding of activator protein-1 is increased in human mesangial cells cultured in high glucose concentrations
AU Wilmer, William A.; Cosio, Fernando G.
CS Division of Nephrology, Department of Medicine, The Ohio State University, Columbus, OH, USA
SO Kidney International (**1998**), 53(5), 1172-1181
CODEN: KDYIA5; ISSN: 0085-2538
PB Blackwell Science, Inc.
DT Journal
LA English
RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Kidney International (**1998**), 53(5), 1172-1181
CODEN: KDYIA5; ISSN: 0085-2538
AB DNA binding of activator protein-1 is increased in human mesangial cells cultured in high glucose concns. Human mesangial cells (HMC) grown in high glucose environments synthesize excessive amts. of extracellular matrix proteins (ECM). The promoter regions of certain ECM genes contain TPA (phorbol ester)-responsive element (TRE) motifs that bind the transcription factor, activator protein-1 (AP-1), a complex of Jun and other phosphoproteins. AP-1 binding to the TRE promoter is regulated by the quantity, composition and post-translational modifications of proteins in the AP-1 complex. We report an increased binding of AP-1 to TRE oligonucleotides in HMC cultured chronically (5 days) in high glucose environments (30 mM D-glucose). This increased binding is not due to differences in the nuclear quantity of AP-1 proteins or in the composition of the AP-1 complex when compared to AP-1 proteins from cells grown in normal glucose (5 mM D-glucose). A 30 mM L-glucose environment also increased AP-1 binding, but to a degree less than D-glucose. The increased AP-1 binding was partly reversed by treatment of HMC with calphostin C or bisindolylmaleimide I suggesting a partial role of the protein kinase C (PKC) pathway in mediating AP-1 binding. AP-1 binding was unaffected by treatment of cells with the MEK inhibitor PD 98059. In addition, increased AP-1 binding persisted for at least 48 h after media glucose concns. were normalized. The level of Jun-N-terminal kinase (**JNK**) activity and the phosphorylation of the **JNK** kinase, SEK1, were unchanged

by chronic high glucose concns. These studies suggest that in HMC cultured in chronic high glucose, post-translational modifications increase the binding of AP-1 to the TRE motif.
ST **diabetes** hyperglycemia mesangial cell AP1

L6 ANSWER 71 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:277795 CAPLUS
DN 128:306907
TI Apoptosis in cardiac **hypertrophy**
AU Aikawa, Ryuichi
CS Fac. Med., Univ. Tokyo, Tokyo, 113, Japan
SO Saishin Igaku (**1998**), 53(5), 1049-1055
CODEN: SAIGAK; ISSN: 0370-8241
PB Saishin Igakusha
DT Journal; General Review
LA Japanese
TI Apoptosis in cardiac **hypertrophy**
SO Saishin Igaku (**1998**), 53(5), 1049-1055
CODEN: SAIGAK; ISSN: 0370-8241
AB A review with 34 refs., on pathophysiol. significance of apoptosis in the mech. stress- and pressure overload-induced cardiac **hypertrophy**. Possible involvement of humoral factors and MAP kinase family (**JNK** and p38MAPK) in the apoptosis is also discussed.
ST review cardiac **hypertrophy** apoptosis MAP kinase
IT Apoptosis
Signal transduction, biological
(apoptosis in cardiac **hypertrophy**)
IT Heart, disease
(**hypertrophy**; apoptosis in cardiac **hypertrophy**)
IT 142243-02-5, MAP kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(apoptosis in cardiac **hypertrophy**)

L6 ANSWER 72 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:233018 CAPLUS
DN 129:335
TI Staurosporine-induced apoptosis in cardiomyocytes: a potential role of caspase-3
AU Yue, Tian-Li; Wang, Chuanlin; Romanic, Anne M.; Kikly, Kristine; Keller, Paul; Dewolf, Walter E.; Hart, Timothy K.; Thomas, Heath C.; Storer, Barbara; Gu, Juan-Li; Wang, Xinkang; Feuerstein, Giora Z.
CS Department of Cardiovascular Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406-0939, USA
SO Journal of Molecular and Cellular Cardiology (**1998**), 30(3), 495-507
CODEN: JMCDAY; ISSN: 0022-2828
PB Academic Press Ltd.
DT Journal
LA English
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Molecular and Cellular Cardiology (**1998**), 30(3), 495-507
CODEN: JMCDAY; ISSN: 0022-2828
AB Cardiomyocyte apoptosis has been demonstrated in animal models of cardiac injury as well as in patients with congestive heart failure or acute myocardial **infarction**. Therefore, apoptosis has been proposed as an important process in cardiac remodeling and progression of myocardial dysfunction. However, the mechanisms underlying cardiac apoptosis are poorly understood. The present study was designed to determine whether the family of caspase proteases and stress-activated protein

kinase (SAPK/**JNK**) are involved in cardiac apoptosis. Cultured rat neonatal cardiac myocytes were treated with staurosporine to induce apoptosis as evidenced by the morphol. (including ultrastructural) characteristics of cell shrinkage, cytoplasmic and nuclear condensation, and fragmentation. Nucleosomal DNA fragmentation in myocytes was further identified by agarose gel electrophoresis (DNA ladder) as well as in situ nick end-labeling (TUNEL). Staurosporine-induced apoptosis in myocytes was a time- and concentration-(0.25-1 μM)-dependent process. Staurosporine-induced apoptosis in myocytes was reduced by a cell-permeable, irreversible tripeptide inhibitor of caspases, ZVAD-fmk, but not by the ICE-specific inhibitor, Ac-YVAD-CHO. At 10, 50 and 100 μM of ZVAD-fmk, staurosporine-induced myocyte apoptosis was reduced by 5.8, 39.1 ($P<0.01$) and 53.8% ($P<0.01$), resp. Staurosporine, at 0.25-1 μM, increased caspase activity in cardiomyocytes by five- to eight-fold, peaking at 4-8 h after stimulation. Based on substrate specificity anal., the major component of caspases activated in myocytes was consistent with caspase-3 (CPP32). Moreover, the appearance of the 17-kD subunit of active caspase-3 in staurosporine-treated myocytes was demonstrated by immunocytochem. anal. In contrast, staurosporine induced a rapid and transient inhibition of SAPK/**JNK** in myocytes. The SAPK activity in myocytes was reduced by 68.3 and 58.3% ($P<0.01$ v basal) at 10 and 30 min after treatment with 1 μM of staurosporine, resp. The results suggest that staurosporine-induced cardiac myocyte apoptosis involves activation of caspases, mainly caspase-3, but not activation of the SAPK signaling pathway.

L6 ANSWER 73 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:223566 CAPLUS
DN 129:14760
TI Stimulation of "stress-regulated" mitogen-activated protein kinases (stress-activated protein kinases/c-Jun N-terminal kinases and p38-mitogen-activated protein kinases) in perfused rat hearts by oxidative and other stresses
AU Clerk, Angela; Fuller, Stephen J.; Michael, Ashour; Sugden, Peter H.
CS National Heart and Lung Institute Division, Imperial College School of Medicine, London, SW3 6LY, UK
SO Journal of Biological Chemistry (**1998**), 273(13), 7228-7234
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO Journal of Biological Chemistry (**1998**), 273(13), 7228-7234
CODEN: JBCHA3; ISSN: 0021-9258
AB "Stress-regulated" mitogen-activated protein kinases (SR-MAPKs) comprise the stress-activated protein kinases (SAPKs)/c-Jun N-terminal kinases (JNKs) and the p38-MAPKs. In the perfused heart, **ischemia**/reperfusion activates SR-MAPKs. Although the agent(s) directly responsible is unclear, reactive oxygen species are generated during **ischemia**/reperfusion. We have assessed the ability of oxidative stress (as exemplified by H2O2) to activate SR-MAPKs in the perfused heart and compared it with the effect of **ischemia**/reperfusion. H2O2 activated both SAPKs/JNKs and p38-MAPK. Maximal activation by H2O2 in both cases was observed at 0.5 mM. Whereas activation of p38-MAPK by H2O2 was comparable to that of **ischemia** and **ischemia**/reperfusion, activation of the SAPKs/JNKs was less than that of **ischemia**/reperfusion. As with **ischemia**/reperfusion, there was minimal activation of the ERK MAPK subfamily by H2O2. MAPK-activated protein kinase 2 (MAPKAPK2), a downstream substrate of p38-MAPKs, was activated by H2O2 to a similar extent as with **ischemia** or **ischemia**/reperfusion. In all instances,

activation of MAPKAPK2 in perfused hearts was inhibited by SB203580, an inhibitor of p38-MAPKs. Perfusion of hearts at high aortic pressure (20 kilopascals) also activated the SR-MAPKs and MAPKAPK2. Free radical trapping agents (DMSO and N-t-butyl-α-Ph nitrone) inhibited the activation of SR-MAPKs and MAPKAPK2 by **ischemia**/reperfusion. These data are consistent with a role for reactive oxygen species in the activation of SR-MAPKs during **ischemia**/reperfusion.

ST SAPK **JNK** kinase p38 MAPK stress; oxidative stress SAPK **JNK** p38 MAPK

IT Heart
Ischemia
Oxidative stress, biological
Stress, animal
(stimulation of stress-regulated mitogen-activated protein kinases (stress-activated protein kinases/c-Jun N-terminal kinases and p38-mitogen-activated protein kinases) in perfused rat hearts by oxidative and other stresses)

IT 146838-30-4 155215-87-5, SAPK/**JNK** kinase 165245-96-5, p38-MAP kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stimulation of stress-regulated mitogen-activated protein kinases (stress-activated protein kinases/c-Jun N-terminal kinases and p38-mitogen-activated protein kinases) in perfused rat hearts by oxidative and other stresses)

L6 ANSWER 74 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:219308 CAPLUS
DN 128:253825
TI Cloning of cDNA for cytokine-, stress-, and oncoprotein-activated human protein kinase kinases and their clinical applications
IN Davis, Roger J.; Gupta, Shashi; Raingeaud, Joel; Derijard, Benoit
PA USA
SO U.S., 58 pp., Cont.-in-part of U.S. Ser. No. 446,083.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5736381	A	19980407	US 1995-530950	19950919	<--
	US 5804427	A	19980908	US 1995-446083	19950519	<--
	CA 2219487	AA	19961121	CA 1996-2219487	19960126	<--
	WO 9636642	A1	19961121	WO 1996-US1078	19960126	<--
	W: AU, CA, JP, KR, MX					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	AU 9649046	A1	19961129	AU 1996-49046	19960126	<--
	AU 710877	B2	19990930			
	EP 830374	A1	19980325	EP 1996-905233	19960126	<--
	EP 830374	B1	20020717			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE					
	JP 2002503946	T2	20020205	JP 1996-534787	19960126	
	AT 220719	E	20020815	AT 1996-905233	19960126	
	EP 1251177	A2	20021023	EP 2002-15784	19960126	
	EP 1251177	A3	20030423			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE					
	PT 830374	T	20021129	PT 1996-905233	19960126	
	ES 2179178	T3	20030116	ES 1996-905233	19960126	
	US 6136596	A	20001024	US 1997-888429	19970707	
	US 6541605	B1	20030401	US 1998-57009	19980407	
	US 6174676	B1	20010116	US 1998-149879	19980908	
	US 6610523	B1	20030826	US 2000-593653	20000613	

	US 2002102691	A1	20020801	US 2001-761569	20010116
	US 2003129606	A1	20030710	US 2002-137953	20020503
PRAI	US 1995-446083	A2	19950519		
	US 1995-530950	A	19950919		
	EP 1996-905233	A3	19960126		
	WO 1996-US1078	W	19960126		
	US 1997-888429	A3	19970707		
	US 1998-57009	A1	19980407		
	US 1998-149879	A1	19980908		
	US 2000-593653	A1	20000613		

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

PI US 5736381 A **19980407**

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5736381	A	19980407	US 1995-530950	19950919	<--
	US 5804427	A	19980908	US 1995-446083	19950519	<--
	CA 2219487	AA	19961121	CA 1996-2219487	19960126	<--
	WO 9636642	A1	19961121	WO 1996-US1078	19960126	<--
	W: AU, CA, JP, KR, MX					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	AU 9649046	A1	19961129	AU 1996-49046	19960126	<--
	AU 710877	B2	19990930			
	EP 830374	A1	19980325	EP 1996-905233	19960126	<--
	EP 830374	B1	20020717			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE					
	JP 2002503946	T2	20020205	JP 1996-534787	19960126	
	AT 220719	E	20020815	AT 1996-905233	19960126	
	EP 1251177	A2	20021023	EP 2002-15784	19960126	
	EP 1251177	A3	20030423			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE					
	PT 830374	T	20021129	PT 1996-905233	19960126	
	ES 2179178	T3	20030116	ES 1996-905233	19960126	
	US 6136596	A	20001024	US 1997-888429	19970707	
	US 6541605	B1	20030401	US 1998-57009	19980407	
	US 6174676	B1	20010116	US 1998-149879	19980908	
	US 6610523	B1	20030826	US 2000-593653	20000613	
	US 2002102691	A1	20020801	US 2001-761569	20010116	
	US 2003129606	A1	20030710	US 2002-137953	20020503	

AB Disclosed are the cDNA encoding human mitogen-activated (MAP) kinase kinase isoforms (MKKs) MKK3, MKK4-α, MKK4-β, MKK4γ (all from brain), and MKK6 (from skeletal muscle). MKKs mediate unique signal transduction pathways that activate human MAP kinases p38 and **JNK**, which result in activation of other factors, including activating transcription factor-2 (ATF2) and c-Jun. The pathways are activated by a number of factors, including cytokines and environmental stress. Methods are provided for identifying reagents that modulate MKK function or activity and for the use of such reagents in the treatment of MKK-mediated disorders consisting of **ischemic** heart failure, kidney failure, etc.

IT 155215-87-5, **JNK** kinase 192230-91-4, **JNK**/p38 kinase kinase
RL: ANT (Analyte); ANST (Analytical study)
(substrate of mitogen-activated protein kinase kinases; cloning of cDNA for cytokine-, stress-, and oncoprotein-activated human protein kinase kinases and clin. applications)

L6 ANSWER 75 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:206104 CAPLUS
DN 129:313
TI Carvedilol inhibits activation of stress-activated protein kinase and reduces reperfusion injury in perfused rabbit heart

AU Yue, Tian-Li; Ma, Xin-Liang; Gu, Juan-Li; Ruffolo, Robert R., Jr.; Feuerstein, Giora Z.
CS Department of Cardiovascular Pharmacology, SmithKline Beecham Pharmaceutical, King of Prussia, PA, 19406-0939, USA
SO European Journal of Pharmacology (**1998**), 345(1), 61-65
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
SO European Journal of Pharmacology (**1998**), 345(1), 61-65
CODEN: EJPHAZ; ISSN: 0014-2999
AB Stress-activated protein kinase (SAPK/**JNK**) has been implicated in the signaling pathway that leads to cell death. Carvedilol, a new vasodilating β-adrenoceptor antagonist with potent antioxidant activity, has been shown to convey a high degree of cardioprotection in a variety of exptl. models of myocardial **ischemia** as well as in patients with congestive heart failure. The present study was designed to explore whether the cardioprotective effects of carvedilol involve inhibition of SAPK activation. Ex vivo **ischemia** (30 min)-reperfusion (60-120 min) of the rabbit heart resulted in 67% reduction of pressure-rate product, 45% necrosis of left ventricular tissue and 62% loss of myocardial creatine kinase ($P<0.01$ vs. basal). SAPK levels in the perfused hearts increased markedly following reperfusion (5.6-fold increase, $P<0.01$ vs. basal). Carvedilol, at 10 μM, administered at time of reperfusion, enhanced recovery of pressure-rate product by 61%, reduced necrotic size by 65% and decreased myocardial creatine kinase loss by 62% ($P<0.01$ vs. vehicle). Carvedilol also inhibited reperfusion-induced activation of SAPK by 61% ($P<0.01$ vs. vehicle). Carvedilol, at 1 μM, displayed a trend of cardioprotection and inhibition of SAPK activation. These results suggest that SAPK may play a role in **ischemia**/reperfusion-induced cardiac injury and inhibition of SAPK activation by carvedilol may contribute to its cardioprotective effects.

L6 ANSWER 76 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:173041 CAPLUS
DN 128:293479
TI Cardiac **hypertrophy** induced by mitogen-activated protein kinase kinase 7, a specific activator for c-Jun NH2-terminal kinase in ventricular muscle cells
AU Wang, Yibin; Su, Bing; Sah, Valerie P.; Brown, Joan Heller; Han, Jiahuai; Chien, Kenneth R.
CS Department of Medicine, University of California at San Diego, La Jolla, CA, 92093, USA
SO Journal of Biological Chemistry (**1998**), 273(10), 5423-5426
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Cardiac **hypertrophy** induced by mitogen-activated protein kinase kinase 7, a specific activator for c-Jun NH2-terminal kinase in ventricular muscle cells
SO Journal of Biological Chemistry (**1998**), 273(10), 5423-5426
CODEN: JBCHA3; ISSN: 0021-9258
AB Activation of stress-activated protein kinases, including the p38 and the c-Jun NH2-terminal kinases (**JNK**), have been associated with the onset of cardiac **hypertrophy** and cell death in response to hemodynamic overload and **ischemia**/reperfusion injury. Upon

infection of cultured neonatal rat cardiac myocytes with recombinant adenoviral vectors expressing a wild type and a constitutively active mutant of MKK7 (or JNKK2), **JNK** was specifically activated without affecting other mitogen-activated protein kinases, including extracellular signal-regulated protein kinases and p38. Specific activation of the **JNK** pathway in cardiac myocytes induced characteristic features of **hypertrophy**, including an increase in cell size, elevated expression of atrial natriuretic factor, and induction of sarcomere organization. In contrast, co-activation of both **JNK** (by MKK7) and p38 (by MIK3 or MKK6) in cardiomyocytes led to an induction of cytopathic responses and suppression of hypertrophic responses. These data provide the first direct evidence that activation of **JNK** alone is sufficient to induce characteristic features of cardiac **hypertrophy**, thereby supporting an active role for the **JNK** pathway in the development of cardiac **hypertrophy**. The cytopathic response, as a result of co-activation of both **JNK** and p38, may contribute to the loss of contractile function and viability of cardiomyocytes following hemodynamic overload and cardiac **ischemia**/reperfusion injury.

ST heart reperfusion injury **hypertrophy** **JNK** p38

IT Heart, disease
(**hypertrophy**; **JNK** and p38 roles in cardiac **hypertrophy**)

IT Reperfusion
(injury; **JNK** and p38 roles in cardiac **hypertrophy**)

IT Heart, disease
(**ischemia**; **JNK** and p38 roles in cardiac **hypertrophy**)

IT Heart
(myocyte; **JNK** and p38 roles in cardiac **hypertrophy**)

IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(p38; **JNK** and p38 roles in cardiac **hypertrophy**)

IT Heart
(ventricle; **JNK** and p38 roles in cardiac **hypertrophy**)

IT 155215-87-5 172308-13-3 192230-91-4, MAP kinase kinase 7 194739-73-6
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**JNK** and p38 roles in cardiac **hypertrophy**)

IT 85637-73-6, Atrial natriuretic factor
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**JNK** and p38 roles in cardiac **hypertrophy**)

L6 ANSWER 77 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:90646 CAPLUS

DN 128:165775

TI Cardiac mitogen-activated protein kinase activities are chronically increased in stroke-prone hypertensive rats

AU Izumi, Yasukatsu; Kim, Shokei; Murakami, Tomohisa; Yamanaka, Shinya; Iwao, Hiroshi

CS Department of Pharmacology, Osaka City University Medical School, Asahimachi, Abeno, Osaka, 545, Japan

SO Hypertension (**1998**), 31(1, Pt. 1), 50-56
CODEN: HPRTDN; ISSN: 0194-911X

PB Williams & Wilkins

DT Journal

LA English

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Hypertension (**1998**), 31(1, Pt. 1), 50-56
CODEN: HPRTDN; ISSN: 0194-911X

AB To examine chronic changes in mitogen-activated protein (MAP) kinases in cardiac **hypertrophy**, the authors determined the activities of two subfamilies of MAP kinases, including extracellular signal-regulated kinases (ERKs) and c-Jun NH2-terminal kinases (JNKs), in the heart of stroke-prone spontaneously hypertensive rats (SHRSP) and Wistar-Kyoto rats (WKY) aged 5, 8, 14, and 24 wk. MAP kinases were determined by using in-gel kinase assay. In both the left and right ventricles of WKY, the activities of ERKs (p44ERK and p42ERK) and JNKs (p46JNK and p55JNK) decreased significantly with age, indicating that aging remarkably downregulated cardiac MAP kinase activities. In SHRSP, left ventricular ERK and **JNK** activities were already significantly higher at the mild hypertensive phase than they were in the same age of WKY, and they remained higher until development of left ventricular **hypertrophy** . On the contrary, the right ventricle of SHRSP, which did not exhibit cardiac **hypertrophy**, had no significant increase in ERK or **JNK** activities compared with WKY, except for the slight increase in p55JNK in 24-wk-old SHRSP. Antihypertensive treatment of SHRSP with imidapril, an angiotensin-converting enzyme inhibitor, decreased the left ventricular **JNK** activities but did not affect ERK activities, suggesting the contribution of hypertension or the renin-angiotensin system to the increase in JNKs. The authors' observations provide the first evidence that both ERK and **JNK** activities are higher in the left ventricle of SHRSP than WKY. However, further study is needed to elucidate the mechanism and the significance of the increased' cardiac MAP kinases in SHRSP.

IT Heart, disease
(**hypertrophy**; cardiac mitogen-activated protein kinase activities are chronically increased in stroke-prone hypertensive rats)

IT Heart, disease
(left ventricle, **hypertrophy**; cardiac mitogen-activated protein kinase activities are chronically increased in stroke-prone hypertensive rats in relation to)

L6 ANSWER 78 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:37392 CAPLUS
DN 128:165802
TI Activation of c-Jun N-terminal kinase during **ischemia** and reperfusion in mouse liver
AU Onishi, Ichiro; Tani, Takashi; Hashimoto, Tetsuo; Shimizu, Kouichi; Yagi, Masao; Yamamoto, Ken-ichi; Yoshioka, Katsuji
CS 13-1 Takaramachi, Cancer Research Institute, Department of Molecular Pathology, Kanazawa University, Kanazawa, 920, Japan
SO FEBS Letters (**1997**), 420(2,3), 201-204
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Activation of c-Jun N-terminal kinase during **ischemia** and reperfusion in mouse liver
SO FEBS Letters (**1997**), 420(2,3), 201-204
CODEN: FEBLAL; ISSN: 0014-5793
AB The authors have generated a mouse model for hepatic **ischemia** in which surgical s.c. transposition of the spleen allows hepatic **ischemia** to be applied without affecting other tissues. Using this mouse model, the authors investigated the relation between the length of **ischemic** periods in the liver and subsequent liver function;

furthermore, the authors assayed the activation of c-Jun N-terminal kinase (**JNK**) during **ischemia** and reperfusion. Although prior to this study only the activated form of **JNK** was known to be translocated to the nucleus, the authors found that **JNK** translocates to the nucleus during **ischemia** without activation and is then activated during reperfusion. These results suggest a novel mechanism of **JNK** activation.

ST cJun kinase liver **ischemia** reperfusion

IT Cell nucleus
(c-Jun N-terminal kinase translocates to the nucleus during hepatic **ischemia** without activation and is then activated during reperfusion)

IT Biological transport
(intracellular; c-Jun N-terminal kinase translocates to the nucleus during hepatic **ischemia** without activation and is then activated during reperfusion)

IT Liver, disease
(**ischemia**; c-Jun N-terminal kinase translocates to the nucleus during hepatic **ischemia** without activation and is then activated during reperfusion)

IT Reperfusion
(of **ischemic** liver; c-Jun N-terminal kinase translocates to the nucleus during hepatic **ischemia** without activation and is then activated during reperfusion)

IT 155215-87-5, **JNK** kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-Jun N-terminal kinase translocates to the nucleus during hepatic **ischemia** without activation and is then activated during reperfusion)

L6 ANSWER 79 OF 102 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:24906 CAPLUS
DN 128:87259
TI Activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury
AU Hu, Yanhua; Cheng, Linda; Hochleitner, Boris-Wolfgang; Xu, Qingbo
CS Institute for Biomedical Aging Research, Austrian Academy of Sciences, Innsbruck, A-6020, Austria
SO Arteriosclerosis, Thrombosis, and Vascular Biology (**1997**), 17(11), 2808-2816
CODEN: ATVBFA; ISSN: 1079-5642
PB American Heart Association
DT Journal
LA English
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Activation of mitogen-activated protein kinases (ERK/**JNK**) and AP-1 transcription factor in rat carotid arteries after balloon injury
SO Arteriosclerosis, Thrombosis, and Vascular Biology (**1997**), 17(11), 2808-2816
CODEN: ATVBFA; ISSN: 1079-5642
AB Smooth muscle cell proliferation is a key event in neointimal formation after balloon **angioplasty**. The mol. signals that mediate this process have yet to be identified. Mitogen-activated protein (MAP) kinases are thought to play a pivotal role in transmitting transmembrane signals required for cell proliferation in vitro. The present studies were designed to investigate whether the signal transduction pathways of MAP kinases were involved in the development of **restenosis** in the injured arteries. Rat carotid arteries were isolated at various time points after balloon injury, and activities of MAP kinases, including